

that the first randomised trials, which were carried out at Guy's Hospital, indicated the need for good local control and the increased mortality from breast cancer which occurred when treatment was sub-optimal. In the first trial (E Series) 374 women aged  $\geq 50$ , with T1, T2, N0 and N1 tumours were randomised to either Halsted mastectomy and post-operative radiotherapy or wide excision and post-operative irradiation. Both groups were given 25–27 Gy to the gland fields and the wide excision group received additionally 35–38 Gy to the breast.

Hence the wide excision group had no axillary surgery and subsequent axillary irradiation using what is now regarded as a low dose of radiotherapy. The first analysis of this trial indicated that increased risk of axillary relapse was restricted to N1 cases and so a second trial was conducted with entry only for those with clinically negative axillae (N0 series). Of 255 cases entered, 133 were randomised to mastectomy and 122 to wide excision. The same radiotherapy schedule was used as in the E Series.

In the E Series, after 25 years follow-up, local relapse occurred in 26% of the mastectomy group and 50% of the wide excision group ( $\chi^2 = 21.6$ ,  $p < 0.001$ ). The breast cancer specific mortality rate at 25 years was 56% in the mastectomy group and 63% in those treated by wide excision ( $\chi^2 = 5.33$ ,  $p = 0.02$ ). For those in the second NO trial, after 25 years local relapse occurred in 18% of the mastectomy cases and 54% of the wide excision group ( $\chi^2 = 30.6$ ,  $p < 0.001$ ). There were significantly more distant relapses in the latter group ( $\chi^2 = 6.32$ ,  $p = 0.01$ ), and a significant increase in breast cancer deaths (57% versus 44%,  $\chi^2 = 4.27$ ,  $p = 0.04$ ).

These two trials, conducted before the widespread introduction of systemic adjuvant therapy, both indicate the long-term effects of inadequate primary treatment. Inadvertent failure to treat the axilla effectively led not only to significantly increased axillary relapse rates but also to more deaths from metastatic disease.

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#### **NSABP Protocol B-06: A randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer – Results after 15 years of follow-up**

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**Background:** Previous reports from Protocol B-06 conducted by the National Surgical Adjuvant Breast and Bowel Project demonstrated the worth of lumpectomy and breast irradiation in the treatment of invasive breast cancer. This report updates the findings through an average of 15 years of follow-up.

**Methods:** Patients with tumors 4 cm or less and either clinically negative or clinically positive axillary nodes were randomly assigned: 1) total mastectomy and axillary dissection, 2) lumpectomy and axillary dissection, or 3) lumpectomy and axillary dissection followed by breast irradiation. There are 1851 eligible patients with known axillary nodal status and follow-up data available.

**Results:** No significant differences were found in overall disease-free survival, distant disease-free survival, or survival between those patients who underwent total mastectomy and those treated by lumpectomy alone or lumpectomy followed by breast irradiation. After 15 years of follow-up, the cumulative incidence of ipsilateral breast tumor recurrence (IBTR) was 36% in the group treated with lumpectomy alone and 12% in the group treated by lumpectomy and breast irradiation.

**Conclusions:** The findings continue to demonstrate that lumpectomy followed by breast irradiation is an appropriate treatment for women with operable Stage I and Stage II invasive breast cancer.

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#### **The Milan experience in surgical strategies for early breast cancer (overview on prospective trials with latest end-results)**

B. Salvadori. *Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy*

This is an up-date of distant results of conservative treatment for breast cancer of limited size (2–2.5 cm in major diameter). Results are dated March 1998, according to the last report of our study control office.

Three different patient series had been entered into controlled randomized studies (Milan I, II, III). The fourth series consists of women conservatively treated in the routine (out-trial patients).

**Milan I** – Halsted Mastectomy vs. QU.A.R.T (Quadrantectomy, Axillary complete dissection and Radiotherapy on the residual gland). Activated

1973. Accrual 1973–1980 – 701 cases (349 vs. 352). Median follow-up 240 months. Overall survival: Halsted 60.1% – QU.A.R.T 59.6. Local Recurrences: Halsted 2.29% – QU.A.R.T 8.2%.

**Milan II** – QU.A.R.T vs. T.A.R.T (T = tumorectomy). Activated 1985. Accrual 1985–1989 – 705 cases (360 vs 345). Median follow-up 126 months. Overall survival: QU.A.R.T 79% – T.A.R.T 77%. Local Recurrences: QU.A.R.T 8.0% – T.A.R.T 19%.

**Milan III** – QU.A.R.T vs. QU.AD (no RT). Activated 1987. Accrual 1987–1989 – 567 cases (294 vs 273). Median follow-up 95 months. Overall survival: QU.A.R.T 88.4% – QU.AD 88.3%. Local Recurrences: QU.A.R.T 4.7% – QU.AD 17.6%.

**Out Trial series** – 1,526 cases treated by QU.A.R.T (1970–1984). Median follow-up 171 months. Overall survival 69.5% Local Recurrences 9.5%.

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INVITED

#### **The impact of local control in early breast cancer. Update of the EORTC trials**

H. Bartelink. *On behalf of the EORTC Breast Cancer and Radiotherapy Cooperative Groups and the Danish Breast Cancer Cooperative Group; Department of Radiotherapy, The Netherlands Cancer Institute, Plesmanlaan 121, 1066CX Amsterdam, The Netherlands*

The EORTC trial 10801 randomized patients with stage I and II breast cancer between radical mastectomy (RM) and breast conserving therapy (BCT). The study included patients with tumors of up to 5 cm with a microscopically incomplete resection. The long term results (median follow-up 13 years) still show that the survival is similar in both treatment arms. In patients with a local recurrence treated with salvage therapy, disappointing local control and survival rates have been observed, both in those initially treated with mastectomy or breast conserving therapy. In order to investigate which patients would benefit from RM or BCT, a joint analysis was performed within the DBCCG, which carried out a similar study making it possible to analyse a total number of 1670 patients. These results showed that patients <35 yrs had a higher local recurrence rate with BCT compared with RM. The number of patients included <35 yrs, however, was very small. In all other patient categories similar local control and survival rates were observed. In the consecutive EORTC trial, investigating the value of a boost dose, which included 5569 patients, young age (<40 yrs) was again one of the major prognostic factors for local control. The major difference between the young age group and the older patient group was the higher number of patients with an initially incomplete excision and smaller volume of the resected breast tissue surrounding the tumor.

Thursday, 1 October 1998

09:30-11:30

#### **SYMPOSIUM**

### **Psychosocial issues in the management of breast cancer**

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#### **Why do cancer doctors burn out and can it be prevented?**

A.J. Ramirez. *ICRF Psychosocial Oncology Group and Department of Liaison Psychiatry, St Thomas Hospital, London, UK*

There is ongoing concern about the mental health of doctors generally. Combining the results of three recent large UK studies, the estimated prevalence of psychiatric morbidity among hospital consultants is 28%. This is similar to levels reported by junior doctors, but clearly in excess of the 18% reported among the employed general population. Cancer doctors appear to be at no greater risk of burnout and psychiatric morbidity than other consultants. This is despite the particular stresses inherent in cancer medicine arising from the frequent exposure to death and dying and the conflict between the curative goals, on which most training is based and the palliative goals of much cancer care.

Across all specialist groups, job satisfaction appears to protect significantly consultants' mental health against the adverse effects of job stress. The predominant source of job stress reported by consultants is overload and its effect on home life. Major sources of job satisfaction include dealing well with patients and relatives, having professional status and esteem, having a high level of autonomy and variety in the job. Feeling insuffi-

ciently trained in communication and management skills increases the risk of burnout among consultants.

These problems need to be tackled in order to reduce the suffering of doctors and their families and minimise the associated risk of impairing the quality of patient care they deliver.

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### The impact of quality of life (QL) scores on survival in patients with metastatic breast cancer (MBC)

Alan Coates. *Australian Cancer Society, Australian New Zealand Breast Cancer Trials Group, University of Sydney and the Internationale Gruppe Lebensqualität in der Onkologie, Australia*

**Purpose:** To investigate the relationship between QL scores and subsequent survival in patients with MBC.

**Methods:** Multivariate regression was performed on survival from the time of QL evaluation including QL scores and other prognostic variables in three separate groups of patients with MBC, from a prospective randomised clinical trial; a multinational cross sectional study; and a detailed single institution psychological assessment. QL scores included Spitzer's QLI, various linear analogue self assessment (LASA) scores and the EORTC QLQ-C30.

**Results:** In all three settings, QL scores were powerful independent predictors of subsequent survival duration.

**Conclusion:** QL captures prognostically useful information about patients with MBC. This may imply that interventions which improve QL would in turn prolong survival. Trials to test this hypothesis are in progress.

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### Treatment decision making in breast cancer: The use of multimedia

S. Molenaar<sup>1</sup>, M.A.G. Sprangers<sup>1</sup>, E.J.T. Rutgers<sup>2</sup>, F.C.E. Postma-Schuit<sup>3</sup>, P. Oosterveld<sup>1</sup>, J.C.J.M. de Haes<sup>1</sup>. <sup>1</sup>Academic Medical Center, Amsterdam; <sup>2</sup>Dutch Cancer Institute, Amsterdam; <sup>3</sup>Comprehensive Cancer Center, Amsterdam, The Netherlands

**Purpose:** A multimedia approach (CDROM) is applied in a decision aid on breast cancer. This program aims to facilitate shared decision making between patients and surgeons in the choice between breast conservation therapy (BC) or mastectomy (M). In an experimental study we are investigating the effectiveness of the CDROM compared to standard information. This abstract addresses preliminary results from patients allocated to the CDROM. We investigated feasibility, patients' ratings with regard to the information provided, influence on decision uncertainty, and on treatment preference.

**Methods:** Patients were assessed at baseline and after program viewing. Self-administered questionnaires were used to measure patients' ratings, decision uncertainty and treatment preference.

**Results:** Ninety-six experimental patients were included. The program was found to be feasible. Patients' ratings of the information provided were very positive. Decision uncertainty was significantly lower after using the CDROM compared to baseline ( $p < .001$ ). Treatment preference at baseline (M 23%; BC 58%; unsure 19%) shifted towards BC after using the CDROM (M 18%; BC 73%; unsure 9%).

**Conclusion:** The CDROM is feasible. Patients reacted positively to the information provided. Within the experimental group decision uncertainty was reduced and treatment preferences shifted towards BC.

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INVITED

### Needs for care in breast cancer patients

J.C.J.M. de Haes, S. Molenaar. *Academic Medical Center, Amsterdam, The Netherlands*

In the Netherlands, the Government Advisory Body for Oncology devised a format 'Guideline for guidelines'. This format is meant to be used as a basis for national guidelines developed by the different tumour working groups active in the country.

For the first time, a systematic approach of psycho-social issues is being advocated in this guideline. The basic psychosocial requirements formulated are divided over four disease phases: 1) the diagnostic phase; 2) curative treatment; 3) follow up; 4) palliative treatment/terminal care. In these phases the following aspects are considered relevant: 1) information; 2) decision making; 3) emotional and social support; 4) supportive care; 5)

continuity of care. These aspects have to be specified for every tumour type addressed in guidelines.

One of the first national guidelines to be developed is the one regarding treatment of breast cancer. A literature search was done to describe the specific psychosocial needs of breast cancer patients. Of the 64 references selected, 33 were related to early detection or epidemiology and therefore not useful. Eight were considered a misclassification. Seven were related to the diagnostic phase, 6 to curative treatment, 4 to follow up and 3 to palliative/terminal care.

The information gathered was far from sufficient to fill in the basic requirements for a psychosocial guideline for breast cancer care. Therefore, the specification of breast cancer patients' psychosocial needs can not solely be based on evidence from the literature. As a result, a process of reaching consensus based on the contribution of patients and professionals should be initiated to fill in the gaps found in the literature.

Thursday, 1 October 1998

11:45-12:30

### PLENARY LECTURE

## Expanding our knowledge of breast cancer biology: will it impact on patient management?

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INVITED

### Expanding our knowledge of breast cancer biology: Will it impact on patient management?

Martine J. Piccart. *Institut Jules Bordet, Unité de Chimiothérapie, Rue Héger-Bordet 1, 1000 Brussels, Belgium*

Many oncologists believe that our growing understanding of breast cancer biology is beginning to translate into

- (1) improved treatment selection for the individual patient, based on determination of predictive molecular markers in the tumor.
- (2) innovative therapies with specific molecular targets in the cancer cell or its environment.

Are these expectations "realistic"?

The purpose of this talk will be to review a number of molecular pathways relevant to breast cancer biology and to highlight, in each case, which components of these pathways are the targets of "predictive factors" studies and/or new therapies.

An attempt will be made 1) at summarizing the complex and rapidly expanding literature regarding the former and the present state of development of the latter, 2) at drawing some conclusions both for daily clinical practice and clinical research.

Anti-neu, anti-ras and anti-invasion therapies will be included in this overview.