

ciated with a poor prognosis in breast cancer. The HER family comprises four receptors (HER1-4) which heterodimerise following ligand binding to activate intracellular signal transduction pathways.

We have studied the four members of this growth factor receptor family in tissue from 220 randomly selected patients who were treated for breast cancer between 1984 and 1993. Follow up data was available for all these patients. Expression was assessed by immunohistochemistry using specific antibodies to each of the family members.

Elevated expression of EGFr (HER1) was observed in 16%, HER2 in 23%, HER3 in 18% and HER4 in 12% of breast cancers. Patients with elevated expression of EGFr, HER2 or HER3 had significantly reduced survival ($p = <0.001$). Patients with high levels of HER4 had increased survival ($P = 0.01$) relative to patients with low levels of HER4. Expression of any 2 of EGFr, HER2, HER3 further reduced survival. HER4 was rarely associated with other members of the HER family (2% of cases). Cox's multiple regression analysis showed that EGFr, HER2, HER3 and HER4 are independent of size and grade and HER2 is independent of stage.

These results show that expression of members of the HER type I receptor tyrosine kinases in breast cancer is more complex than investigation of individual members of the family may suggest. Combinations of HER1-3 can further impact on patient prognosis. The role of HER4 remains poorly understood and the mechanism underlying the apparent prolonged survival in patients expressing this protein is not known. The development of agents specifically targeted against HER2 (Herceptin), EGFr (Iressa) and members of the downstream signalling pathways activated by the HER family provide new possibilities in the treatment of breast cancer. However the complex interactions highlighted by this study further suggest that we should be taking a pathway oriented approach to analysis and treatment of breast cancer

O-64. THE PROGNOSTIC VALUE OF CONTRALATERAL, METACHRONOUS, AND BILATERAL, SYNCHRONOUS BREAST CANCER IN BREAST CANCER PATIENTS

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In the Twente-Achterhoek region breast conservative treatment (BCT) is the treatment of choice since 1984 for patients with T1 and T2 (3 cm breast carcinoma). Until 1998 1545 patients with breast cancer were treated with BCT.

Forty-four patients presented with an already treated tumour in the contralateral breast. Forty patients presented with bilateral, synchronous breast cancer (BBC). Sixty-three patients developed contralateral breast cancer (CBC) in the follow-up. The follow-up ranged from 3 to 206 months with a median of 68 months. A significant relation was seen between CBC and the different clinical and histopathological factors such as age, family history, and histology. From the 63 patients with CBC 17.5% was (40 years

($p = 0.009$), and 36.5% had a positive family history ($p < 0.001$), compared to 8.1% and 20.1% respectively for the rest. This was in contrast to BBC where no significant relation was seen to clinical and histopathological factors.

The overall recurrence rate was 34.9% for CBC and 30% for BBC compared to 16.2% for the rest ($p < 0.001$ and $p = 0.021$). The local recurrence rate was respectively 17.5% and 3.6% for CBC versus the rest ($p < 0.001$), and the distant metastasis rate respectively 25.4% versus 14.6 % ($p = 0.016$). Only the distant metastasis rate was significantly higher for BBC versus the rest ($p = 0.006$).

In a multivariate logistic regression analysis for the presence of distant metastasis for BBC, taking into account all relevant factors, bilaterality did not show significance (O.R. 2.1; 95% Conf. Interval 0.7–5.6; $p = 0.163$).

In a multivariate logistic regression analysis CBC was the strongest factor for local recurrence (O.R. 5.2; $p < 0.001$; 95% Conf. Interval 2.4–11.3).

The 5-year disease specific survival for the 63 patients with CBC versus the rest was 92.4% versus 91.3% respectively. For the patients with BBC this was 81.5% compare to 91% for the rest of the patients (log rank $p = 0.0017$).

The 5-year local recurrence free survival (LRFS) was 88.9% for patients with CBC and 97% for the rest ($P < 0.001$). In a multivariate Cox-regression analysis for LRFS, taking into account all relevant factors contralaterality did show significance (H.R. 3.1; 95% Conf. Interval 1.5–6.2; $p = 0.002$).

The 5-year disease free survival (DFS) for BBC versus the rest was 72.3% and 85.6% respectively (log rank, $p = 0.011$). In a multivariate Cox-regression analysis for DFS, taking into account all relevant factor bilaterality did not show significance (H.R. 1.6; 95% Conf. Interval 0.7–3.6; $p = 0.279$).

Conclusion: This study shows a difference in predictive factors and prognostic value for patients with CBC or BBC versus unilateral breast cancer. The presence of BBC seems to have no major prognostic value. There is a significant relation between CBC and local recurrence.

O-65. IMMEDIATE BREAST RECONSTRUCTION USING THE LATISSIMUS DORSI MYOCUTANEOUS FLAP (LDF): LONG TERM RESULTS AT 15 YEARS PLUS

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Although early results of immediate reconstruction using LDF are satisfactory, long term consequences are not well known. The aim of this study was to assess by questionnaire the effects of immediate breast reconstruction 15 years plus after the procedure. Between 1983 and 1995 78 patients underwent a mastectomy and immediate reconstruction using LDF. In 1987, 47 were surveyed by questionnaire (EQ) (exclusion: 11 deceased, 5 lost to follow up, 15 non-responders). In December 2000 33 of the 47 took part in a later questionnaire (LQ) (exclusion 6 deceased, 2 lost to follow up, 6 non-responders). In this longitudinal study

patients were used as their own controls for changes in time. Statistical comparisons were made by using McNemara's exact test for paired data to detect significant changes between patient responses for before mastectomy, EQ and at LQ, the chi-squared test to test for significant changes in muscular function and cosmesis and the Wilcoxon signed rank test for cosmetic ratings.

33% of patients reported restrictions in ipsilateral arm movements in EQ. Statistically there was no improvement with time. Symmetry was maintained in 33% at 15 years but most patients preferred to forego further revision surgery. Most patients considered the back scar satisfactory, 61% reported it as hidden by the bra strap. Over 50% of patients reported abnormal sensation in the flap and area surrounding it. Pain and discomfort significantly reduced with time. This method of reconstruction was highly satisfactory from the patients' viewpoint with 91% feeling it was worth performing.

In spite of significant restriction of arm movements and asymmetry persisting even after 15 years, most patients were satisfied with their operation.

O-66. A SINGLE INSTITUTIONAL EXPERIENCE WITH SENTINEL NODE BIOPSY IN 400 BREAST CANCER PATIENTS

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Introduction: The technique of lymphatic mapping in breast cancer can spare patients an axillary lymph node dissection (ALND) and stage these patients more accurately. The aim of our study was to evaluate the results of sentinel node biopsy at our institution.

Patients and Methods: From January 1997 to November 2000, 400 consecutive patients with cT1-2N0 breast cancer were studied. The first 82 patients underwent confirmatory ALND. Five patients had a bilateral tumor and 49 patients a non-palpable tumor. The mean histological tumor diameter was 1.9 cm (0.3–8.0) with a pT1 stage in 65.8%, pT2 in 33.9% and pT3 in 0.3%. Preoperative lymphoscintigraphy was performed after injection of Tc-99m-nanocolloid into the tumor in a volume of 0.2 ml and a mean radioactive dose of 2.6 mCi (1.1–4.3). The sentinel node was surgically identified with the aid of patent blue dye (1.0 ml, intratumoral injection) and a gamma-ray detection probe. Sentinel nodes were step-sectioned and stained with H&E and immunohistochemistry (CAM5.2). The median follow-up of patients without ALND after a tumor-negative sentinel node was 11 months (range 1–23)

Results: In 369 of 405 procedures (91%), a sentinel node was visualized during lymphoscintigraphy. The sentinel lymph node was intraoperatively identified in 386 procedures (95%). Pathological examination showed sentinel node metastases in 155 cases. The sentinel node was false negative in four patients corresponding to a sensitivity of 97.5%. Two false negative results were based on routine ALND, one was established through intraoperative palpation and excision of a firm and tumor pos-

itive non-sentinel node and one patient developed an axillary recurrence 22 months postoperatively. The sentinel node was not found in 19 patients. Fifteen of these patients underwent ALND (tumor-positive in 7) and 4 received radiotherapy of the axilla. A sentinel node outside level I or II of the axilla was visualized in 106 patients (27%). Internal mammary chain nodes could be harvested in 84% and other non-axillary sentinel nodes in 89% of the patients. The pathological status of non-axillary sentinel nodes changed further treatment in 24% of patients with non-axillary drainage.

Conclusion: Sentinel node biopsy seems to be a highly accurate technique although the follow-up of patients without confirmatory axillary lymph node dissection is short. Excision of sentinel nodes outside level I and II of the axilla can accomplish more precise staging.

O-67. DOES AXILLARY NODE SAMPLING IN ADDITION TO SENTINEL NODE BIOPSY PROVIDE USEFUL STAGING INFORMATION IN PATIENTS WITH BREAST CANCER?

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The aims of this study were to determine if: 1) axillary sampling (AS) in addition to sentinel node biopsy (SNB) reduces the false negative rate of SNB alone. 2) AS predicts those patients with remaining axillary node metastases following a positive SNB.

From a series of 66 patients undergoing SNB using radio-isotope and Patent Blue V dye, in the last consecutive 38 patients we performed an AS after SNB followed by a completion level II axillary dissection (AD).

Sentinel nodes were identified in 36/38 cases (94.7%); 22 were negative and 14 positive. When validated against AD however there were 3 false negatives (3/17 = 17.6%). Of these, 2 had clinically involved nodes at surgery, but the other false negative was also "missed" by AS. The false negative rate therefore for SNB + AS was 1/17 (5.9%). Of the 14 positive SNB, 7 had further nodal disease in the axilla - in 4 cases this was detected by AS but in the remaining 3 the AS was clear.

SNB is unreliable in the presence of obviously involved nodes and additional AS reduces the false negative rate of SNB alone in this situation whilst AS of clinically uninvolved nodes however does not improve staging. A negative AS following a positive SNB does not exclude the need for further axillary treatment.

O-68. BLUE AND HOT HITS THE SPOT- OR DOES IT NOT? COMPARABILITY OF A FOUR NODE SAMPLE TO SENTINEL NODE BIOPSY

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Of 1180 published studies nearly all suggest the use of SLNB in breast cancer. None have sufficient statistical power; the majority is based on series of less than 40 node positive patients. A study