

N+ status (1 to 7 positive nodes), patients are randomised between FNC and simultaneous locoregional radiotherapy (arm A) or FEC (Epirubicin 60 mg/m²) followed by radiotherapy (arm B). After age 50, recommended attitude of hormone therapy is to give tamoxifen 20 mg daily, whatever the tumor hormonal status.

Methods: Primary end point is 5 years Disease Free Survival (DFS). Secondary objectives are loco-regional recurrence, immediate and late toxicity and quality of life (EORTC QLQ-C30). To show 0.10 discrepancy between 5 years DFS (0.65 vs 0.75), 650 patients are required ($\alpha = 0.05$, 2 sided, $\beta = 0.20$). Stratified randomisation is done according to the center (11 centers), the number of positive nodes (1–3/4–7) and the type of surgery (tumorectomy/mastectomy). No interim analysis is planned.

Results: This trial began in December 1994 and is still going on, involving 502 patients up to January 98 (251/251). The inclusions will be closed at the end of 1998. Tumorectomy is realised for 2/3 of the patients and the number of nodes involved is 1–3 for 80% of them. There is no imbalance between the two arms in term of clinical and histologic factors. The patients follow-up is obtained at 4 months for 80% (A) vs 71% (B), and at one year for 59% (A) vs 53% (B).

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POSTER

Does the administration of anthracyclines affect human tumour blood flow?

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Introduction: The use of anthracycline-containing drug regimens is increasing in both the neoadjuvant and adjuvant treatment of breast cancer. Tumour blood flow is an important parameter in treatment outcome. Studies in mice bearing human tumour cell lines have shown that administration of doxorubicin can consistently reduce regional blood flow as measured by laser Doppler flowmetry. Reduced blood flow may compromise the delivery of subsequent drugs reducing the efficacy of treatment or alternatively may potentiate the effects of bioreductive agents such as mitomycin C.

Aim: To investigate the effect of anthracycline administration on human tumour blood flow.

Methods: Six consecutive females undergoing neoadjuvant chemotherapy for primary breast cancer were studied. Patients received either FEC (5-fluorouracil 600 mg/m², epirubicin 60 mg/m² and cyclophosphamide 600 mg/m²) or MM (methotrexate 35 mg/m² and mitoxantrone 11 mg/m²). Up to 6 laser Doppler microprobes were inserted into the primary tumour mass and blood flow was recorded for 10 minutes pre-and for up to 60 minutes post-epirubicin or mitoxantrone administration (and prior to the other drugs).

Results: Blood flow has been analysed in 5 patients. Considerable inter- and intra-tumour variability has been seen with no consistent trend demonstrated so far.

Conclusions: This technique can be used to measure human tumour blood flow after administration of chemotherapy. Results from this study may influence patient management by identifying which tumours may benefit from the addition of blood-flow modifying agents to the anthracycline-containing regime.

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POSTER

Ocular toxicity related to tamoxifen therapy

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Previously published cases suggest that tamoxifen has a potential for causing ophthalmologic toxicity, with retinal, corneal, and optic nerve abnormalities. We analyzed 260 postmenopausal women with operable, No, breast cancer and tried to determine the prevalence of ocular toxicity-after tamoxifen therapy. One group (130 subjects) was treated with 10–20 mg tamoxifen daily, and the other (E0 subjects) with 20–40 mg. All of them underwent slit lamp anterior segment examination and fundal examination with direct ophthalmoscopy.

In the 1st, there were 2 cases of central (muscular) retinopathy (total tamoxifen dose 32.4 g and 39.8 g). In the 2nd group, there was 1 patient with corneal opacities, 1 with macular oedema, 1 with optic neuritis. Cumulative doses for the 3 were 29.8 g, 37.6 g, and 42.3 g, respectively.

Both conventional and high dose tamoxifen can cause ophthalmologic complications, as shown in the study, requiring regular ophthalmologic examinations for those on long term tamoxifen.

Thursday, 1 October 1998

16:00-18:00

PARALLEL SESSION

Surgery

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INVITED

Breast cancer patients treated without axillary surgery: Clinical implications and biological analysis

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Until now axillary dissection has been considered an integral part of breast cancer treatment. However, we believe that axillary surgery can be avoided in selected breast cancer patients. 401 breast cancer patients (mean age 62.9 years) underwent breast surgery without axillary dissection from January 1986 to June 1994, principally considering age, and small tumour size. No patients had clinically involved nodes in homolateral axilla. 216 out of 401 patients (53.6%) had a pathological tumour diameter ≤ 1 cm, 133 (33.6%) were between 1 and 2 cm, whereas 38 (9.5%) had a tumour size > 2 cm. The histological diagnosis was ductal infiltrating carcinoma in 188 cases (46.9%), associated to DCIS in 73 cases (18.2%). LIC was present only as histotype in 59 cases (14.7%). Breast conservative surgery was performed in 383 patients (95.6%) and only 18 patients (4.4%) underwent total mastectomy in consideration of the presence of extensive intraductal component. 257 patients (64.1%) received radiotherapy to the operated breast. In elderly patients an adjuvant hormone therapy was preferred considering the hormonal receptorial status.

An accurate updated follow-up > 36 months was obtained in all patients (mean 58.5 months, range 36–122); 58 patients died, 32 for uncorrelated or unknown causes. 29 (7.2%) patients had distant metastases only and 6 (1.5%) patients had axillary and distant metastases synchronously. 28 (6.9%) patients had clinically axillary metastases as only and first site of metastatic disease: 28 patients underwent full axillary dissection showing pathological metastases in 21 cases. The mean number of metastatic nodes was 6 (1–32) and the mean diameter of the primary tumour in these metastatic cases was 16.8 mm. Only one case had a tumour diameter < 1 cm. The mean time of disease free interval was 29.1 months. 3 patients out of 34 were treated with radiotherapy to the axilla without surgery, and 3 patients were treated with hormone therapy. 17 out of 28 operated patients are disease free. Considering the present results, some pathologic, biologic and clinical parameters were retrospectively investigated on the primary tumours of this series, in order to identify an alternative criteria, excluding the nodal involvement, for giving an adjuvant treatment. The results allow to recognize a biological subpopulation of tumours with high risk of distant relapse, independently from the axillary nodal status. This study is not a prospective randomized trial, however we can conclude that avoiding axillary dissection does not impair local control of disease and does not have a negative impact on long term outcome in selected patients. However, the risk could be an undertreatment of the patients after the breast cancer surgery, due to the lack of information on the axillary nodes for planning adjuvant treatment. The research of alternative parameters on the primary tumours by which planning adjuvant treatments will give the possibility of a better control of distant relapse also sparing the axillary nodes.

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ORAL

Preoperative MRI does not influence the amount of breast tissue excised in conservative cancer surgery

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Aim: Breast magnetic resonance imaging (MRI) provides accurate information about tumour size and location which correlate closely with histological size. Clinical assessment of tumour size is very variable and often overestimates histological size. We assessed prospectively the impact of MRI information on extent of surgical resection.

Method: 96 patients with breast cancer diagnosed by triple assessment, underwent breast conservation surgery over 1 year. Of these patients 29 underwent pre-operative MRI using a T1-weighted 3D FLASH sequence. MRI images were not used for decision-making on type of surgery but were shown to the operating surgeon pre-operatively to indicate the location of the lesion and its local extent. Clinical information and histological assessment

were compared between those patients who underwent pre-operative MRI and those who did not. Excision margins were considered to be involved if the closest margin measured less than 1 mm.

Results: 96 of 134 patients underwent wide local excision or segmental resection (72%) over a 1 year period. There was no significant difference between the MRI group (n = 29) and no-MRI group (n = 67) in excision margin positivity rates (31% v 29%; p = 0.81) or average specimen weight (91 g ± 71 v 95 g ± 88; mean ± SD). Re-excision for histologically confirmed residual disease was performed in 8 patients. Three patients (10% of MRI group) had a pre-operative MRI and 5 did not (7% of no-MRI group).

Conclusion: Our results suggest that MRI does not currently influence the margin or volume of surgical excision in breast conservation and that surgeons are still primarily guided by their clinical assessment of local extent.

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ORAL

Preoperative assessment of axillary lymph-node involvement in small breast cancers. Analysis of 893 cases

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Purpose: To predict histological axillary involvement risk (pN+) before surgery.

Methods: In 893 patients with infiltrating carcinoma (TOT1T2 ≤ 3 cm) treated by lumpectomy, axillary dissection and radiotherapy from 1980 to 1991, 6 parameters were analysed.

Results: Global pN+ rate was 25.3%. According to the 6 parameters, we noted:

Clinical size (T)	T0	T1	T2		
	13.8%	19.8%	36.6%		
Histological size (pT) (mm)	0-9.9	10-14.9	15-19.9	20-24.9	25-29.9
	11.1%	17.7%	26.5%	30.1%	36%
Histological subtype	SBR1	SBR2	SBR3	LIC	Other
	18.3%	27.2%	37.8%	22.7%	10%
Age	<40	40-60	>60		
	30.3%	25.8%	22.4%		
Breast size	Small	Large			
	30.1%	24.4%			
Topography	Inner	Central	Outer		
	20.1%	24.4%	28.8%		

After a multivariate analysis, only three factors were significant for pN+ risk: T (p < 0.0001), histological subtype (p = 0.0005) and breast size (p = 0.004). With a combination of these three factors, the pN+ rates vary from 5% to 50%.

Conclusions: Both clinical and pathological characteristics of the primary tumor (specified by core biopsy) can define the pN+ risk, and select the candidates for limited axillary surgery by sentinel node.

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ORAL

Conservation surgery and specialist treatment

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Introduction: The nature of the survival advantage associated with treatment at centres with larger case-loads and a specialist interest remains uncertain. We report the results of a retrospective study comparing the use of conservation surgery and recurrence rates in specialist and non-specialist units.

Methods: All women aged under 75 diagnosed in a defined geographical area in the West of Scotland were identified for the years 1986-91. From all case-records available (2411, 85% of total), details of operative procedures, pathology, adjuvant therapy and recurrence were obtained.

Results: Specialists compared to non-specialists rarely performed conservation surgery on tumours greater than 3 cm (4% vs 16%, p < 0.001), rarely breached tumour margins (2.5% vs 10%, p < 0.001), rarely performed multiple operations (2% vs 6%, p < 0.001), less frequently left positive margins (5% vs 12%, p < 0.001), re-excised positive margins more frequently (7.5% vs 2.6%, p < 0.001), omitted radiotherapy less frequently (16% vs 32%, p < 0.001) and had recurrence rates significantly lower (10% vs 17%, p < 0.001).

Conclusions: We conclude that specialist treatment using conservation surgery has been more rational, in keeping with guidelines and has resulted in a significantly fewer number of local recurrences.

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ORAL

Are risk factors for local and distant recurrence following breast-conserving therapy for early breast cancer similar to those following mastectomy?

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Purpose: Risk factors for local recurrence and distant disease after breast-conserving treatment (BCT) and mastectomy were compared by pooling the data of two randomized clinical trials for stage I and II breast cancer patients, trial 10801 of the EORTC and trial 82TM of the Danish Breast Cancer Cooperative Group (DBCG).

Methods: The total number of patients included in the study was 1670: 832 had received modified radical mastectomy and 838 BCT, comprising local excision, axillary dissection, 50 Gy whole breast irradiation and a boost to the tumor bed. Representative slides of the primary tumor were obtained for review for 1508 patient.

Results: There were 73 patients with local recurrence after BCT and 72 after mastectomy, 10-year rates being 10% and 9% respectively. Patients ≤ 35 years (RR = 9.9) and patients with extensive intraductal component (EIC) (RR = 2.7) had a significantly higher risk of local recurrence after BCT, but not after mastectomy. Lobular carcinoma (RR = 2.9) was associated with a higher risk of local recurrence after mastectomy. Patients with tumours of high histologic grade or showing vascular invasion were at an increased risk of local recurrence, irrespective of the type of primary treatment.

Conclusions: From the viewpoint of local control mastectomy may be preferred for patients ≤ 35 years and for those with EIC; and certainly if these factors are combined. The high risk of local recurrence after BCT for patients ≤ 35 years warrants further study to rule out any negative impact of breast-conservation on survival in individual patients. Histologic grade and the presence of vascular invasion appear to be of little importance regarding the choice between BCT and mastectomy.

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ORAL

The characteristics and management of extremely elderly patients with breast cancer

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Purpose: The surgical management of elderly patients is still controversial. We examined the characteristics and clinical outcome of extremely elderly patients who were 80 years of age and older and suffering from breast cancer.

Methods: We studied the cases of 45 extremely elderly patients who underwent surgery in our hospital between 1966 and 1995. 1) We evaluated the changes in the prevalence of extremely elderly patients on a 10 year basis. 2) Clinical features were evaluated in comparison with patients younger than 80 years of age who underwent surgery during the same period. 3) Extremely elderly patients were divided into two groups: one group consisted of those who underwent axillary dissection (group A, 16 cases), the other consisted of those without axillary dissection (group B, 20 cases). Five-year and 10-year survival rate were analyzed retrospectively.

Results: 1) Extremely elderly patients increased decennially both in number (10 to 32) and proportion (1.2% to 2.0%). 2) Elderly patients tended to include more advanced cases with stage III and IV compared with those younger than 80 years of age (14/45 vs 596/2891, p < 0.08), and also tended to include more ER positive cases (23/30 vs 892/1459, p < 0.08). 3) Five-year survival rate was 66% and 10-year survival rate was 49% in group A. Five-year survival rate was 79% and 10-year survival rate was 40% in group B. Although this study was performed retrospectively, tumor size, breakdown of stages, ER positive rate and use of adjuvant therapy were not different between the two groups.

Conclusion: Axillary dissection is not necessary in extremely elderly patients.