812 POSTER

Can scintimammography predict axillary involvement in breast cancer?

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Introduction: Axillary dissection is a standard procedure which provides breast cancer staging and prognostic information, and part of therapy. However, as earlier disease detection occurs, fewer patients will have nodal involvement. Identification of patients who are node negative is important to reduce morbidity, prevent lymphoedema of the arm, and reduce costs. A variety of imaging techniques including mammography, ultrasound scanning with colour Doppler, and liposomal scintigraphy have been tried with poor specificity. A new scintigraphic technique using Tc-99m Sestamibi has been used to identify axillary nodal involvement.

Patients and Methods: Scintimammography was carried out in 93 patients who subsequently underwent a level II axillary dissection. The standard Khalkhali-Diggles regimen was used injecting 740 MBq of Tc-99m Sestamibi into a foot vein. Imaging started after 5 minutes and the axillae were imaged both anteriorly and laterally.

Results: Scintimammography correctly predicted the lymph nodal status in 64.5% of patients (37 true positive, 23 true negative, 10 false positives, 23 false negative). While large nodal masses showed uptake in all patients, small lesions were not imaged.

Comment: Our results show that large nodal masses may be imaged using Tc-99m Sestamibi scintimammography. However, since it is unlikely that an imaging modality will show up a small tumour, scintimammography in its current form is unlikely to be clinically useful in detecting a small nodal deposit. Therefore, whilst scintimammography has a complementary place in the diagnosis and management of breast cancer, sentinel node biopsy is recommended to confirm nodal involvement in the axillae. Assessment of the sentinel node will save a large number of women unnecessary surgery.

813 PUBLICATION

Locally advanced breast cancer (LABC): Neoadjuvant chemotherapy with sequential doxorubicine (DOX) and docetaxel (DOC)

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Introduction: DOX and DOC are considered as the best single agents in advanced breast cancer with response rates ranging in first line from 38–52% and from 50–65% respectively, and in second line from 15–29% and 40–55%. Both compounds are devoid of total cross-resistance. We present here the preliminary results of monotherapy with DOX followed by single agent DOC, given as neoadjuvant regimen in 20 patients with LABC.

Patients and Methods: Between 06/97 and 11/98, 20 patients (4 stages IIIa; 16 stages IIIb) were included in the trial and received first 2 cycles of DOX 75 mg/m^2 (q3w), followed by 2 cycles DOC 100 mg/m^2 (1 hour infusion, q3w). Clinical, biochemical and radiological response was evaluated after 2 and 4 cycles. Thereafter, loco-regional treatment was administered and further systemic treatment was planned according to the observed response.

Results: By clinical evaluation according to the UICC criteria, 16 pts had objective regression (5 CR, 11 PR), 4 had stabilization. Six pts who showed no response after 2× DOX, responded clearly after 2× DOC. There were no serious complications. Dose reduction during 2nd course of DOC (75%) was only necessary in 2 pts because of mucositis (1) and myalgia (1). After completion of neoadjuvant chemotherapy, local treatment consisted of exclusive radiation therapy (RT) in 2 pts and surgery followed by RT in 18 pts. Pathological examination in the latter showed disappearance of invasive tumor at the primary site in 5 pts (3 had persisting DCIS). Subsequent systemic therapy was adapted to the initial ER status (tamoxifen for ER or PR+), and to the pathological axillary nodal status (adjuvant chemotherapy if N+).

Conclusions: We conclude that a high response rate can be achieved within 12 weeks with the proposed regimen, which proved to be very well tolerated. This regimen is worth being compared to others for inducing response in LABC.

814 PUBLICATION

Intraoperative radiotherapy (IORT) in breast cancer – A high quality boost in breast conserving therapy

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Purpose: After breast conserving surgery and radiotherapy, the majority of local recurrences occurs in the vicinity of the former primary tumor site. The geographic miss of the tumor bed is a well documented phenomen in boost irradiation, demanding adequate techniques of high quality boost set-ups.

Methods: From 10/98 until 2/99, conservative surgery was performed in 18 patients with stage I or II breast cancer in a dedicated IORT facility. After tumorectomy, the tissue surrounding the excision hole was temporarily approximated by sutures for IORT. Depth dose prescription was done by intraoperative sonography of the tumor bed. A single fractional dose of 9 Gy was applied to the 90% reference isodose with electron energies ranging from 4–12 MeV (Philips SL 18). After wound healing, patients presenting with ductal carcinoma received 51Gy EBRT of the whole breast, patients with lobular histology were treated up to 56 Gy. No additional boosting is performed.

Results: In a dedicated unit, the use of IORT prolongues the surgical procedure by only 15–20 minutes, while shortening the duration of the EBRT by 1–2 weeks. Direct visualisation of the tumor bed guarantees the highly accurate delivery of boost doses. There were no early complications associated with the use of IORT. Compared to conventional boost strategies, integral treated volumes are low.

Conclusion: In Salzburg, IORT of the tumor bed is integrated into breast conserving cancer treatment as standard procedure in a prospective study.

815 PUBLICATION

Breast cancer and pregnancy: The Gustave Roussy Institute experience

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Purpose: We conducted a retrospective study of patients whose breast cancer was diagnosed during pregnancy or immediately following delivery

Aims: To investigate how patients were treated and propose a protocol according to the stage and the timing of the pregnancy.

Methods: Patients were treated from 1956 to 1998. Among 57 cases reviewed, 49 were eligible. They were either entirely treated in our institution or referred for advice.

Of the 49 patients, 14 were in the first trimester, 18 in the second, 8 in the third trimester, and 9 cancers were diagnosed after delivery. 24 patients had stage IIIa and B (48%), 18 had inflammatory disease.

Results: From 1956 to 1998, there was a wide variety of treatments with no specific protocol. The prognosis remained quite poor (52% mortality rate).

Conclusion: As the association of breast cancer and pregnancy is becoming more frequent, a real protocol should be initiate with neoadjuvant chemotherapy from the forth month of pregnancy, since it has been demonstrated that such treatment does not induce foetal abnormalities.

816 PUBLICATION

Sentinel node biopsy in breast cancer – The ALMANAC trial

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Aim: The single most important prognostic indicator in the management of breast cancer is the status of the axillary nodes. To enable optimal treatment, all patients with breast cancer undergo an axillary sampling or clearance, with its associated morbidity. The introduction of Sentinel Node Biopsy (SNB) in breast cancer promises to confine an axillary procedure to patients who have a positive SNB.

Methods: We have localised the sentinel node (SN) using a combination of patent blue V and radioisotope. The preoperative injection of nanocoll is followed by lymphoscintigraphy and a hand held probe at surgery is used to locate the SN. At surgery patent blue V dye is injected around the tumour and a blue lymphatic is traced to a blue node. The SN, once localised is

removed and this is followed by primary surgery for the breast cancer and an axillary node clearance.

Results: We have performed this procedure in 64 patients so far and were able to localise the SN in 61 patients (95.3%). Forty seven of the 62 patients (75.8%) had a hot node on scan and in 51 of the 61 patients (79.7%) a hot node was detected using a hand held probe. Fifty five patients had a blue node (85.9%). Twenty three patients had a positive SN. One patient who had a negative SN, had further disease in the axilla resulting in a false negative rate of 4.2%.

Conclusion: We conclude from our early results that the sentinel node in breast cancer can be accurately localised using a combination of methods and that it is an accurate predictor of the axillary node status. The Medical Research Council has funded a two phased, randomised trial in the UK – the ALMANAC trial – which will commence shortly.

817 PUBLICATION

The comparative randomised study of adjuvant therapy of breast cancer patients with tamoxifen versus tamoxifen plus chemotherapy

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Purpose: Between 4/94 and 4/97 103 breast cancer pts, pT1c-3a, pN0-1, M0, preferably postmenopausal, were randomized after radical surgery to adjuvant tamoxifen or to tamoxifen plus CMF (C 500 mg/m^2, M 40 mg/m^2 and F 600 mg/m^2 days 1 and 8 q 28) for 6 cycles. The median age, tumor size, no. of involved lymphnodes (1–3), estrogen receptor status, grade and type of surgery were well balanced among the 50 tamoxifen and the 53 tamoxifen plus CMF pts.

Results: Toxicity either hematological and non-hematological was higher in the group with chemotherapy except weight gain (52% in both group).

Toxicity	TAM	TAM + CMF	
Hematological	0%	32%	(max. leucopenia G II)
Non-hematological	0%	20%	(alopecia + cystitis + alteration of liver function)

After median follow-up of 42 mos. 5 relapses in tamoxifen (locoregional 1, lung 1, bone 1, lung and bone 1, lung, bone and brain 1) and 7 in tamoxifen plus CMF group (locoregional 3, lung 1, bone 1, lung and bone 1, lung, bone and brain 1) were observed (p = NS). The projected 3-y DFS is 92% for tamoxifen and 88% for tamoxifen plus CMF pts. (p = NS). The 3-y OS is 88% for tamoxifen and 80% for tamoxifen plus CMF pts. (p = NS).

Conclusions: both regimens seems to be equale effective with higher toxicity in the group with combined hormonal and chemotherapy.

818 PUBLICATION

The effects of adjuvant chemotherapy on alpha5-beta1 integrin expression of keratinocytes and on wound fibronectin level

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Aim: To evaluate the potential effects of adjuvant chemotherapy (AC) for breast cancer on wound healing at the cellular level.

Methods: In this prospective study, we have studied healing in an in vivo wound model. Patients with invasive, node-positive carcinoma of the breast, receiving Cyclophosphamide, Methotrexate and 5-FU were biopsied on day 8 and day 13 of the first cycle. Biopsies were snap frozen in liquid nitrogen and analysed by immunohistochemical staining. The results were compared against biopsies from age-matched healthy volunteers.

Results: At the time of writing, 6 patients were studied (Age range: 34–56). All wounds had healed by the end of three weeks. Wound re-epithelialisation was delayed as compared to healthy volunteers (n = 6) and the wound matrix was more friable. The alpha5-beta1 Integrin expression seemed to be unaffected in the patients receiving AC. However, the level of Fibronectin within the provisional wound matrix was found to be less than the controls.

Conclusion: (1) Chemotherapy does not seem to have an effect on the keratinocyte expression of alpha5-beta1 Integrin. (2) The observed decrease in the level of Fibronectin may account for the delay in wound re-epithelialisation and friability of wound matrix.

819 PUBLICATION

Second malignancies after LH-RH analogues treatment for early breast cancer

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The appearance of new primary tumours in women operated on breast cancer and treated with adjuvant chemo and/or ormonotherapy (tamoxifen) has been described by many Authors with a 5 years incidence between 1.7 and 4.2%.

We report the experience of our Institute about 81 premenopausal women between 31 and 50 years of age with operable breast cancer treated with adjuvant Goserelin depot administered s.c. every 28 days for two years after surgery, in order to induce pharmacological castration. No patient received cytotoxic therapy before diagnosis of second primary tumour.

After a median follow-up of 60 months we observed 7 new primary tumours: 1 contralateral breast cancer, 2 chronic myeloid leukemias, 1 Hodgkin lymphoma, 1 kidney adenocarcinoma, 1 small cell lung cancer, 1 ovary cancer. All new primaries were hystologically confirmed. The second malignancies developed between 10 and 60 months after diagnosis of breast cancer. It is to be estabilished on one hand the influence of this therapy and on the other how much environmental, occupational or genetic factors could have been contributed to the development of these second tumours.

820 PUBLICATION

Increased total dose and intensification of cyclophosphamide (C), adriamycin (A) and fluoracil (F) regimen for the treatment of breast cancer with involved nodes

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Introduction: The beneficial of adjuvant chemotherapy have been well established for patients (pts) with node-positive breast cancer. The intensity of the regimen is determined by the number of involved axillary lymph nodes. This study compared the combination CAF in pts with 1–3 positive nodes (pn) to sCAF in pts with 4–9 pn.

Methods: From December 1990 to March 1998, 79 pts with node positive breast cancer had received chemotherapy with CAF regimen. In pts with 1–3 pn the treatment consisted of C 500 mg/m^2, A 50 mg/m^2 and F 500 mg/m^2, every 3 weeks for 6 courses (standard CAF) and, in pts with 4–9 pn consisted of C 600 mg/m^2, A 60 mg/m^2 and F 600 mg/m^2 every 3 weeks for 3 courses (sCAF),

N0 pn	Drugs (mg/m^2)	Dose (mg/m^2/wk)	Dose Intensity (mg/m^2)	Total dose
1–3	CAF			
	C and F	500	166.6	3000 mg/m^2
	A	50	16.6	300
4–9	sCAF			
	C and F	600	200	3600
	A	60	600	360

Results: Median follow up was 37 months (5–81). 3 year DFS and 5 year DFS was 74% and 65% in pts with 1–3 pn and 75% and 64% in pts with 4–9 pn, respectively. A total pf 440 cycles were infused with a dose intensity >95% of 63% (CAF) and 52% (sCAF): The inceidence of WHO grade 3–4 toxicity was 6.6% with CAF and 10% with sCAF. The mayor toxicity was myelosuppresion and nausea-vomiting. Neutropenic fever was seen in 0.8% of cycles and 1 congestive heart failure was observed in sCAF group.

Conclusion: Total dose and dose intensity have a significant effect on DFS in the adjuvant treatment of primary breast cancer with involved nodes. SCAF is a safe regimen and may be administered over multiple cycles in ambulatory pts with excellent clinical tolerance.