Poster Sessions

Breast cancer

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The sentinel node procedure in early breast cancer under local anaesthesia

C.L.H. van Berlo[1], H.A.M. Gerritsen[2], R.F.M. Schapers[3]. [1] *St. Maartens Gasthuis, Surgery, Venlo, The Netherlands;* [2] *St. Maartens Gasthuis, Nuclear Medicine, Venlo, The Netherlands;* [3] *St. Maartens Gasthuis, Pathology, Venlo, The Netherlands*

Introduction: Sentinel lymph node (SN) dissection is a highly accurate method of axillary staging in patients with early breast cancer. Patients without SN metastases will not need axillary dissection with its complications and morbidity. After the learning curve in our hospital (1997 -1998; 4% false negatives) and with an experience of more than 200 SN procedures in general anaesthesia, we offer our patients with proven breast cancer (< T4) the possibility of SN detection under local anaesthesia in an out-patient setting.

Patients and methods: From september 2000 until april 2001 58 women with proven breast cancer and without clinical evidence of axillary node involvement underwent a sentinel node procedure under local anaesthesia after informed consent. Preoperative lymphoscintigraphy in two planes was used to mark the sentinel node(s). 1 mC 99mTc-nanocolloid (18 hrs prior to the operation) and 0.5 cc patent blue (5 minutes before incision) were injected intradermally. The SN was identified intraoperatively under local anaesthesia (15 cc prilocaïne 1%) using the blue color and a handheld gamma-probe (Neoprobe 2000). After excision histopathologic examination including immunohistochemistry was performed. In the group with positive SN's an axillary dissection was added to the breast surgery in the same general anaesthesia.

Results: Lymphoscintigraphy enabled us to identify SN's in 56/58 women (97%). In all 58 patients the SN('s) were found using blue dye and gamma-probe (discovery 100%).The SN was positive in 19/58 patients (33%). Two of these (3%) were only detected with immunohistochemistry. In the patients with a positive SN the axillary dissection showed in 4 of 19 cases (21%) another (non-sentinel) positive node. The only complication encountered in the overall group was a haematoma.

Conclusions: A 100% detection of sentinel nodes in early breast cancer harvested under local anaesthesia was achieved without serious morbidity. This two-step procedure (SN under local anaesthesia/definitive breast surgery in general anaesthesia) enables a more individual approach in the surgical management of the patient with early breast cancer. It is less expensive and enables better operative planning. The two-step procedure saved 33% of the patients one general anaesthesia, while still 67% of our patients did not need an axillary dissection.

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Value of additional staging following tumour positive sentinel node (SN) biopsy in breast cancer

P.C. Baars[1], S. Meijer[2], R. Pijpers[1], O.S. Hoekstra[1], G.J.J. Teule[1]. [1] *Vrije Universiteit Medical Centre, Nuclear Medicine, Amsterdam, The Netherlands;* [2] *Vrije Universiteit Medical Centre, Surgical Oncology, Amsterdam, The Netherlands*

Purpose: SN biopsy is a minimally invasive method for axillary staging in breast cancer. Following a positive result, i.e. if the SN contains tumour, additional staging in the form of liver ultrasound (US) and bone scintigraphy (BS) is often performed. We evaluated the yield of the US and BS in SN positive patients in our clinic.

Methods: From 1994-2000, 140 patients with a T1 and T2 tumour had a positive SN biopsy. All had a level I-III axillary dissection resulting in 1 positive lymph node in 81, 2 in 22, 3 in 7 and >3 in 21 patients, the SN included. An US and BS were obtained within 4 weeks following the SN biopsy.

Results: Initial postoperative staging resulted in 21 (US) and 29 (BS) patients where additional imaging was advised. None of the imaging procedures resulted in exposure of metastatic disease. In three patients biopsies (2 from the liver, 1 from the bone) were performed that were negative. The follow up period since surgery has been 34±20 (median 31) months. Four patients developed distant metastases after 18, 39, 45 and 48 months in bone (3x), liver (1x) and lung (1x). In none of these the metastases could be predicted on the basis of initial postoperative staging.

Conclusion: Additional staging following a tumour positive SN biopsy in T1 and T2 breast cancer is unnecessary and not cost effective.

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Interphase cytogenetics with DNA-probes for chromosome 8 to detect circulating tumor cells in breast cancer patients

B.M. Ghadimi[1], J. Uhr[2], T. Tucker[2], K. Heselmeyer-Haddad[3], T. Ried[3], H. Becker[1]. [1] *University Medical Center Goettingen, Dept. of General Surgery, Goettingen, Germany;* [2] *Institute of Immunology, Southwestern Medical Center, Dallas, U.S.A;* [3] *National Cancer Institute, Dept. of Genetics, Bethesda, U.S.A*

Purpose: The detection of micrometastases in the bone marrow or peripheral blood of cancer patients is increasingly used for a more sensitive tumor staging and prognostication. We tried to develop a new approach for the detection of circulating tumor cells in breast cancer patients combining immunomagnetic enrichment and interphase cytogenetics.

Methods: In a blinded study, we have analyzed matched pairs of primary breast cancers and circulating tumor cells from the same patients, isolated with immunomagnetic enrichment, with interphase cytogenetics for chromosome 8.

Results: After analyzing 27 patients with benign as well as malignant breast tumors we can demonstrate that the chromosomal pattern between malignant tumor and corresponding circulating tumor cells is identical. Furthermore, the detection of circulating tumor cells directly correlates with the primary tumor stage. We did not find any cells with chromosome 8 alterations in the patients with benign disease. Surprisingly, even in early breast cancers (T1N0) interphase cytogenetics identified circulating tumor cells in 2 out of 4 patients.

Conclusion: Interphase cytogenetics represents a non-invasive, sensitive and specific assay for the direct visualization of circulating tumor cells in the peripheral blood. The prognostic value of these findings remains to be further evaluated in larger prospective studies.

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Neoadjuvant chemotherapy paclitaxel + doxorubicin (PD) vs fluorouracil + doxorubicin + cyclophosphamide (FAC) in locally advanced breast cancer: Clinical and pathological response

V.F. Semiglazov, A.A. Bojok, A.S. Arsumanov, O.A. Ivanova, V.G. Ivanov, V.V. Semiglazov, K.M. Pozharissky, E.E. Topuzov, K.S. Nurgaziev, R.M. Paltuev. *N.N. Petrov Research Institute of Oncology, 197758 St.-Petersburg, Russia*

Purpose: The aim of study is to test efficacy of PD regimen vs FAC (clinical and pathological response, breast-conserving surgery rate).

Methods: 57 patients (pts) with locally advanced breast cancer (T2N2, T3N1, T4N0-1) received 4 cycles of neoadjuvant chemotherapy-Paclitaxel 200 mg/m^2 + Doxorubicin 60 mg/m^2 (PD-regimen), every 3 weeks (29 pts) vs 4 cycles of neoadjuvant 5-Fluorouracil 600 mg/m^2 + Doxorubicin 60 mg/m^2 + Cyclophosphamide 600 mg/m^2 (FAC), every 3 weeks (28 pts). Tumour response to preoperative chemotherapy was assessed after 4 cycles by palpation and mammography. Then appropriate surgery was performed. Surgical specimens were examined for the presence of microscopic residual tumour.

Results: From October 1999 to December 2000 57 pts were included (29-PD group, 28-FAC). Pathological complete response (pCR) was ob-

Clinical tumour response:

Preoperative treatment	Complete response	Partial response	Stabilization	Progression
Paclitaxel + Doxorubicin (PD)	34.4%	51.7%	13.7%	0
FAC	10.7%	60.7%	28.5%	0

served in 8 pts (27.5%), received PD, and only 2 pts (7.1%), received FAC (P = 0.003). Conservative surgery was realized in 10 pts (34.4%) in PD group and 8 pts (28.5%) in FAC group (P > 0.05).

Conclusion: Primary treatment of locally advanced breast cancer with Paclitaxel + Doxorubicin more effective than FAC regimen in rate of clinical and pathological complete response. Study is ongoing.

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Sentinel nodes outside level I- II of the axilla and staging in breast cancer

R. Rönkä[1], E. Leppänen[2], L. Krogerus[3], K. von Smitten[1], M. Leidenius[1].
[1] *Helsinki University Hospital, Breast Surgery Unit, Helsinki, Finland;*
[2] *Helsinki University Hospital, Unit of Nuclear Medicine, Helsinki, Finland;*
[3] *Helsinki University Hospital, Department of Pathology, Helsinki, Finland*

Purpose: In many centres preoperative lymphatic mapping and sentinel node biopsy has become a routine method for axillary staging in breast cancer. Previous studies have reported sentinel nodes outside level I-II of the axilla (ExAx) in approximately 20% of breast cancer patients. The role of ExAx sentinel node biopsy in staging of breast cancer is still obscure. The aim of the study was to evaluate the incidence of ExAx sentinel nodes in breast cancer patients. The other purpose was to evaluate the success rate and the complications of ExAx sentinel node biopsy. The third aim was to investigate the incidence of metastases in the ExAx and other hand in the axillary sentinel nodes.

Patients and methods: Between June 2000 and April 2001, 172 clinically node-negative T1-T2 breast cancer patients were submitted to lymphatic mapping and sentinel node biopsy. Lymphoscintigraphy was performed the day before surgery, four hours after intratumoral injection of 80-100 MBq 99m nanocolloid.

Results: Lymphoscintigraphy showed altogether 55 sentinel nodes outside level I-II of the axilla in 30 (18%) patients. Two (1%) patients had only ExAx sentinel nodes in the lymphoscintigraphy. The 55 ExAx nodes included 36 parasternal, 9 subclavicular, 7 intramammary and 1 interpectoral nodes. Altogether 39 (71%) extra-axillar nodes were harvested in 26 (87%) patients. Two (7%) of the 30 patients had metastases in ExAx sentinel nodes only, 3 (10%) in both ExAx and axillary nodes and 9 (30%) in axillary nodes only while 16 (53%) patients had metastases in neither axillary nor in ExAx sentinel nodes. Minimal perforation of parietal pleura occurred in three (10%) patients. They recovered uneventfully without pleural drainage.

Conclusions: Harvesting of the ExAx sentinel nodes is technically more demanding compared to the axillary ones, but does not seem to carry considerable risks for the patients. The ExAx sentinel node biopsy is a potential tool for more accurate staging in breast cancer, because it provides more information compared to axillary staging alone.

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A phase III trial of taxotere and doxorubicin (AT) versus 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) in patients with unresectable locally advanced breast cancer: an interim analysis

K. Bouzid[1], J. Vinholes[2], F. Salas[3], E. Mickiewicz[4], S. Valdivia[5], V. Ostapenko[6], E. Baltali[7], N. Ghilezan[8], A.L. Courtin[9], N. Badri[10]. [1] *Pierre et Marie Curie Centre, Algiers, Algeria;* [2] *Santa Casa de Misericordia de Porto Alegre Hospital, Porto Alegre, Brazil;* [3] *IPSS-Guillermo Almenara Irigoyen Hospital, La Victoria, Peru;* [4] *Angel Rofo Institute, Buenos Aires, Argentina;* [5] *Neoplasia National Institute, Lima, Peru;* [6] *Lithuanian Oncology Centre, Vilnius, Lithuania;* [7] *Hacettepe Unviersity, Medical oncology, Ankara, TurkeyNapoca Radiotherapy Oncology, Bucarest, Romania;* [9] *C&AC, Le Kremlin-Bicltre, France;* [10] *Aventis pharma International, Antony, France*

Aim: This study evaluated the efficacy and safety of AT versus FAC, as neo-adjuvant therapy in patients (pts) with stage IIIA T3 or IIIB unresectable locally advanced breast cancer.

Methods: Between February 1999 and September 2000, 407 chemo-naive patients were randomly assigned to either doxorubicin 50mg/m2/15min followed by taxotere 75mg/m2/1h or 5-fluorouracil 500 mg/m2/bolus, doxorubicin 50 mg/m2/15min and cyclophosphamide 500 mg/m2/bolus, given every 3 weeks for 4 cycles. Clinical and pathological responses, and safety were assessed.

Results: To date, interim data are available for 362 patients treated with AT (n=198) or FAC (N=164). Pts in both arms were well balanced for known prognostic factors; median age was 48 years [range: 23 - 75] and median WHO PS was 0 [range: 0 - 1]. A total of 1380 cycles were administered; median number of cycles was 4 [range: 1 - 4] in both arms, and median Relative Dose Intensity was = or > 98,9% for all drugs. In the 362 patients analysed, the overall response rate was 72% for AT [95% CI: 65 - 78] and 64% for FAC [95% CI: 56 - 71]: 11% CR with AT versus 9% with FAC; 61% PR with AT versus 55% with FAC (p=0,11). Information available for 170 patients (AT: 100 pts, FAC: 70 pts) indicate that 92% of AT pts and 89% of FAC underwent surgery. Analyses on pathological response rates are ongoing. Median progression free survival, at the time of this analysis, was 8.3 months for AT [95% CI: 6.2 - 9.1], and 6.9 months for FAC [95% CI: 4.3 - 12.9]. Main treatment-related toxicities seen respectively in AT/FAC arms (% of pts): Grade 3/4 neutropenia (71/25); febrile neutropenia (10/0); Grade 3/4 nausea (6/5); Grade 3/4 vomiting (6/8); Grade 3/4 diarrhea (7/1); Grade 3 stomatitis (2/0); Grade 3/4 infection (3/0); Grade 3 asthenia (3/1).

Conclusion: The safety profile is favourable in both arms. Neutropenia was the most common adverse event but was predictable and manageable. Interim efficacy data are encouraging, suggesting that taxotere and doxorubicin is a potentially valuable combination in neo-adjuvant therapy of breast cancer.

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Phylloide tumours of the breast 36 year revision based on clinical experience

C. Cruz[1], M. Pereira[1], P. Messias[3], N. Cunha[2], J. Ganho[1].
[1] *IPOFG/CROC, Surgery, Coimbra, Portugal;* [2] *IPOFG/CROC, Clinical Pathology, Coimbra, Portugal;* [3] *HDFF, Surgery, Figueira da Foz, Portugal*

The authors realized a 36 year retrospective study of phylloide breast tumours treated at the Portuguese Oncological Institute - Coimbra, based on clinical diagnosis, histopathological and therapeutical aspects.

The study took place during 2 distinctive periods, the first during 1995 - 2001, where 113 clinical cases were analysed. The second during 1965 -1995, where after careful revision and update of the new histopathological criteria of tumours of 113 patients, only 82 were selected; totalising a final number of 195 patients. The histopathological criteria used to classify and select the tumours were those proposed by Page et al.

Results: Of the 195 patients selected, 68,4% had benign tumours, 25,4% borderline tumours and 6,2% malignant tumours. The study showed that the age of primary occurrence was greatest at the following age groups [16-25 yrs] 30% and [30-50 yrs] 43%. The onset period of time was 14,31 months (SD ± 22,15). On average the tumours measured [2-3 cm] 27% and [4-6 cm] 17%. The tumour lateralization was not statistically significant. In 93% of the cases there were associated fibroadenomas. FNAB was positive for phyllodes tumors in 20,9% of the cases.

Of the different surgical approaches studied, wide local excision was by far the most preferred (96,5%), followed by Modified Radical Mastectomy (1,8%), Simple Mastectomy (0,9%) and finally Quadrantectomy (0,9%). The reiterative operations were performed, 3 operations (2,6%), 2 operations (6,1%) and single operation (91,2%). The recurrence rate studied was 13,4% and the free period of disease was 39,19 months (SD ± 19,94). As far as the parity we verified that 42% were nullipare and 58% primipare and multipare.

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Testosterone, an hormonal marker for breast cancer in postmenopausal women(PM): preliminary results of a case-control study in Montreal

J. Latreille[1], M. Falardeau[2], G. Martin[2], A. Robidoux[2], J.M. Ekoe[2], J. Cantin[2], E. Nassif[2], M. Poljicak[2], M. Dumont[3], P. Ghadirian[2].
[1] *cicm-Hopital Charles LeMoyne, Greenfield Park;* [2] *CHUM, centre de recherche, MontrÈal;* [3] *Corev, Outremont, Qc, Canada*

Purpose: Breast cancer is a major health problem associated with a high morbidity in many of the more developed countries of the world. It seems that environmental risk factors and lifestyle play important role in the etiology of this disease. We have yet to find a marker that will have an impact in the prediction of breast cancer occurrence. Methods: In a case-control study in Montreal, a total of 70 newly diagnosed PM with breast cancer and