Interpretation error in both, mammography and breast sonography may lead to delayed diagnosis of breast cancer.

Recognition of these various factors should help decrease the rate of false-negative mammograms.

404 POSTER

Hormonal receptor status and HER2 expression in correlation between age, pathological type, mammographical and ultrasound view of breast cancer treated in oncology clinic of military medical academy, Warsaw, Poland.

M. Gornas[1], E. Pienkowska[1], W. Kozlowski[2], P. Wisniewski[2], J. Sieluzycka[3], P. Gornas[4], C. Szczylik[1]. *[1] Military Medical Academy, Oncology Clinic, Breast Pathology Unit; [2] Military Medical Academy, Pathology Department, Warsaw, Poland; [3] Military Medical Academy, Radiology Department, Warsaw, Poland; [4] Kredyt Bank SA, Out - Patient Clinic, Warsaw, Poland*

Introduction: The aim of the study was to determinate the correlation between biological characteristic of breast cancer, age of patients, mammographical findings and/or ultrasound view of lesions. The question is, if radiogram or ultrasound view of the lesion could help the treatment planning in different groups of patients.

Material and Methods: We have analysed case reports of 116 breast cancer patients treated in Breast Pathology Unit (BPU) of Oncology Clinic since The 1st of January 2000 till the 30th of October 2001. All of patients have become radical modified mastectomy. In most of cases hormonal receptor status and HER-2 expression in breast cancer tissue were determined using immunohistochemical assay. Retrospectively mammographical and ultrasound pictures have been analysed.

Results: 116 breast cancer patients, age 35-81 (average 57) have started treatment in BPU since the 1st of January 2000 till now. In 16 of cases HER-2 expression couldn't be determined (mostly because of technical problems). HER-2 overexpression was found in 32 cases. In 15 of these cases no hormonal receptors were found, in 17 of them ER or/and PR were positive. ER anr/orPR positive cancers were found most frequently (23/32) in the group of 51-60 years old women, then (10/20) over age of 70. In our material HER-2 overexpression most frequently (3/4) was detected in breast cancer patients 30-40 of age, less frequently (3/20) in the group over 70 years old. Most of HER-2 positive cases (14/32) were determined as infiltrating ductal carcinoma, 10/32 mixed (DCIS and invasive component), 2/32 lobular, 1/32 mucinosus, 1/32 apocrinal, 4/32 DCIS. HER-2 positive cases have been found in "dense breast", but the mammographical and ultrasound views were differentiated in most of cases.

Conclusion: The age of patients could be one of circumstances correlating with biological characteristic of breast cancer. Neither mammography, nor ultrasound examination is sufficient for anticipation of treatment planning in breast cancer.

Friday, 22 March 2002 16:30–18:00

PROFFERED PAPERS

Clinical implications of the sentinel node

405 ORAL

Quality control in the EORTC-AMAROS (after mapping of the axilla: radiotherapy or surgery) trial nr 10981

P.S. Verduijn[1], R.L.J.H. Bourez[1], E.J.T. Rutgers[1], V. Distante[2], C.J.H. van de Velde[3]. *[1] The Netherlands Cancer Institute, Surgery, Amsterdam, The Netherlands; [2] Florence, Surgery, Florence, Italy; [3] Leiden University Medical Centre, Surgery, Leiden, The Netherlands*

Introduction: The EORTC-AMAROS trial is a phase III randomised non-inferiority trial comparing a complete ALND versus RT to the axilla in SNB positive patients, where-as SNB patients will be followed for the end-points of the study as well. The involved patients will have an operable invasive breast cancer of over 5 mm and less than 3 cm, without clinically suspected regional lymph nodes. Quality control constitutes an important part of the trial design.

Methods: Before a participating centre is allowed to enter patients, at least 30 SN procedures have to be performed, with a minimum of 27 patients with accurate SN identification. After 30 cases, the centre will be visited and all cases will be reviewed. If quality criteria are not fulfilled, the learning phase will be extended by steps of 10 patients until the last 30 patients have met the criteria. The quality of RT will be controlled by evaluation of a dummy run and an annual evaluation of the filed radiation data of 10 randomly chosen patients done by the RT co-ordinator (or an independent representative).

Amendments: Two amendments were made. One amendment concerned the learning phase of the SN procedure. It states that if a surgeon has performed 30 SNB procedures without ALND under the guidance of a surgeon who has performed at least 30 SNB procedures followed by ALND in accordance to the criteria mentioned in the protocol, this surgeon is also allowed to enter patients in the trial. The other amendment concerned adjuvant systemic treatment. Stating that different schemes (of adjuvant treatment) on the basis of the number of positive nodes are allowed, but not recommended.

Results: Until 1-11-01, 13 sites have been site-visited. Three site visits are planned of which 1 is a second control visit taking place 1 year after the initial visit. During this second visit the records of the included patients will be compared with the matching CRF's. Encountered problems before approval were: -Difficulties in producing an adequate radiotherapy dummy-run (n=4), -Inadequate surgical SN procedure (n=1), -Inadequate probe (n=1), -Inadequate lymfoscintigraphy technique (n=1). So far 6 centres are including patients, the other 7 are being assessed or solving problems to meet all criteria. The total amount of patients included at 1-11-01 equals 111. Result and solutions to prevent problems on the on-site visits will be presented.

406 ORAL

Sentinel node biopsy performed under local anesthesia in early-stage breast carcinoma; the experience of the European Institute of Oncology

G. Gatti[1], A. Frasson[1], C. Magalotti[1], P. Naninato[1], S. Michelini[2], S. Zurrida[1], P. Veronesi[1], V. Galimberti[1], P. Arnone[1], A. Luini[1]. *[1] European Institute of Oncology, Senology Division, Milan, Italy; [2] European Institute of Oncology, General Director, Milan, Italy*

The practice of sentinel node biopsy has dramatically changed the surgical approach to early-stage breast cancer. The impact of this technique on patients' quality of life and on treatment costs, without compromising oncological information, allowed the application of the biopsy to a large population of patients. At the European Institute of Oncology in Milan we recently applied sentinel node biopsy under local anesthesia to a selected group of patients, to verify the feasibility of this procedure and its impact on our therapeutic pathway in case of early-stage breast carcinoma.

From September 2000 till November 2001, 102 patients affected by infiltrating T1/T2-N0 breast tumor received sentinel node biopsy under local anesthesia at the European Institute of Oncology in Milan, Italy. These patients had a citologically/histologically proven infiltrating, unifocal breast carcinoma with a maximum diameter of 2,5 cm. There was no clinical and ultrasonographic evidence of axillary node involvement by the disease. Patients were injected with a mixture of colloidal human albumin particles marked with 99m-Technetium the day before surgery or the same day at a distance of few hours in the Nuclear Medicine Division. Sentinel node was identified using a gamma probe and removed during a surgical session performed under local anesthesia; it was then examined both with extensive histology and immunohistochemistry.

No patients suffered of immediate or late surgical complication. No cases of postoperative axillary haematoma or infection were observed in the days and weeks after sentinel node biopsy. All patients were able to undergo conservative surgery for the breast carcinoma 7-8 days later, with no delay due to problems deriving from the node biopsy. Also the cost analysis we performed showed a good impact of sentinel node biopsy performed under local anesthesia on total treatment costs both for the Institute and the patients.

Our experience indicates that sentinel node biopsy performed under local anesthesia can be a good alternative to standard intra-operative evaluation of the sentinel node in patients with an unifocal, early stage breast carcinoma citologically or histologically proven at the moment of the hospitalization.

407 ORAL

Frozen sections on sentinel lymph nodes: Comparison of two methods

K. Leena[1], M. Leidenius[2], T. Toivonen[1], K. Von Smitten[2]. [1] *Department of Pathology;* [2] *Breast Surgery Unit, Maria Hospital, Helsinki University Hospital, Helsinki, Finland*

Aim of the Study: We started our sentinel node (sn) programme using the frozen sectioning method described by Veronesi and his co-workers[1] (method A). We felt however uneasy about cutting up all the lymph node (ln) tissue as frozen sections, and therefore created our own method of investigation, that involves slicing the ln-with a razor blade before freezing (method B). We now compare the methods of sentinel ln investigation.

Patients and Methods: 207 consecutive clinically T1-T2, node negative breast cancer cases that underwent lymphatic mapping and sn biopsy with frozen section diagnosis were included in the study. The sn:s in the first 104 cases were examined by method A and the last 103 with method B. Patients in both groups were similar as regards to median age, histological tumour size, tumour histology, tumour location, tumour grade, the number of examined axillary ln:s (when axillary clearance was done) and the number of sn:s found.

Results: Sentinel node metastases were found in 28 (27%) patients in group A and in 42 (40%) patients in group B ($p = 0.05$). The sn(s) was the only metastatic nodes in 18 (64%) in group A and in 28 (68%) in group B. The median number of metastatic 1n:s in patients with axillary involvement was 2 (1–7) in group A and 1 (1–14) in group B. The median size of the sn metastases was 5.5 mm (0.5n–16 mm) in group A and 3.3 mm (0.1–15 mm) in group B. The proportion of metastases under 2 mm in size of the sentinel node metastases in groups A and B were 16 and 6 respektively. The false negative rate in frozen section diagnosis was 14% (six cases) in group B and none in group A.

Conclusions: Method B detected more and smaller ln metastases. Defining a minimum size for a metastasis and its relevance for the patient is to be done.

408 ORAL

Clinical implications of internal mammary sentinel node (IM-SN) biopsy

F.W.C. van der Ent[1], R.A.M. Kengen[2], H.A.G. van der Pol[2], J.A.C.M. Povel[1], H.J.G. Stroeken[1], A.G.M. Hoofwijk[1]. [1] *Maaslandziekenhuis, General Surgery, Sittard, The Netherlands;* [2] *Maaslandziekenhuis, Nuclear Medicine, Sittard, The Netherlands*

Introduction: Adjuvant treatment protocols are based on the axillary lymph node status, recognized as the most important prognostic factor in breast cancer. The internal mammary (IM) nodal status is regarded as a second important prognostic factor, since IM-metastases are associated with poor prognosis. Recently, we have demonstrated that routine IM-SN biopsy is feasible. By introducing IM-SN biopsy, more accurate staging could improve survival.

Material and Methods: We report the results and clinical implications of an ongoing prospective study of SN biopsy in 470 consecutive patients. Axillary and IM-SN biopsy was performed using 370 Mbq 99mTc nanocolloid injected peritumorally and 1 ml Patent Blue intradermally. Lymphoscintigraphy showed IM-hotspots in 21% (100/470). IM-SN biopsy was attempted in all cases and was successful in 65% (65/100), revealing IM-metastases in 20% (13/65). In 5% (3/65) of these patients axillary SN biopsy was negative. In 7% (7/100) a small pleural lesion resulted from IM-SN biopsy, which healed uneventfully in all cases.

All IM-SN positive patients received adjuvant chemotherapy, changing systemic treatment in two out of three axillary node-negative patients. Additionally, all IM-SN positive patients received adjuvant parasternal radiotherapy, altering adjuvant treatment in 13% (13/100) of patients with visualized IM-hotspots.

Conclusion: Routine IM-SN biopsy revealed IM-metastases in 20% of successful IM-SN biopsy, resulting in altered adjuvant regimens in 13% of patients with visualized lymphatic drainage patterns to the IM-chain. These patients might gain a survival advantage with a modified adjuvant treatment protocol.

409 ORAL

Sentinel node biopsy in breast cancer: a complete immunohistochemical study

N. Beechey-Newman[1], H. Hamed[1], J. Ajayi[2], I. Fentiman[1]. [1] *Guy's & St. Thomas' Hospitals, Academic Oncology, London, United Kingdom;* [2] *Guy's & St. Thomas' Hospitals, Hedley Atkins Unit, London, United Kingdom*

Background: Sentinel node biopsy (SNB) has been shown to be a very accurate predictor of axillary node status in primary breast cancer. More intensive histological assessment of the sentinel node (SN) such as serial sectioning and immunohistochemistry can reveal occult metastases and increases the sensitivity of SNB. Applying these techniques to the SN alone and at the same time treating all of the non-SNs in a conventional way results in serious scientific bias that over estimates the true sensitivity of SNB.

Methods: Three hundred unselected (T1-3, N0-1) consecutive patients with primary breast cancer were submitted to sentinel biopsy followed by level III axillary clearance. SN localisation was by isotope (0.1ml nanocol, intra-dermal, lymphoscintigram) and dye (0.5 - 1.0ml patent blue V, intradermal) in 112 patients and dye only in 188 patients, the distribution being dependent on the availability of nuclear medicine facilities on the day of surgery and the consent of the patients. All sentinel and non-sentinel nodes were treated identically by serial sectioning followed by H&E and immunohistochmistry for cytokeratin (CAM 5.2).

Results: Out of the total 300 patients a SN was identified in 250 (83.3%). Identification was facilitated by the use of both isotope and dye (91.9%) compared to dye alone (78.2%). A mean of 1.46 SNs and 22 non-SNs were retrieved. In the 250 women who had an identifiable SN this was found to predict the status of the rest of the axilla in 228 giving an accuracy of 91.2% and a sensitivity of 82.3%. There was no difference in the sensitivity of SNB between the methods of localisation used (isotope and dye 84.6%, dye alone 81.1%). Logistic regression analysis including age, histology, tumour grade, size, site, nodal status, needle localisation, previous excision biopsy and dye volume demonstrated that needle localisation of the tumour and high node positivity (less than or equal to 4 positive nodes) was the only factor to be associated with reduced SN identification. None of the same patient or methodological factors analysed affected SNB accuracy.

Conclusions: In this prospective study when patients are not selected and all of the axillary nodes are cleared and treated by similar histological techniques the accuracy and sensitivity of SNB is not as accurate at predicting the status of the axilla as generally quoted. Different patient variables and affect the rate of identification of the SN but not its accuracy.

410 ORAL

Intraoperative cytologic imprint to evaluate sentinel lymph node status

C. Couture[1], S. Jacob[1], R. Dubé[1], L. Provencher[2], J. Robert[2], C. Desbiens[2], J. Lebrun[3], C. Blanchette[4]. [1] *CHA Hôpital Saint-Sacrement, Anatomopathologie et Cytologie, Québec, Canada;* [2] *CHA Hôpital Saint-Sacrement, Chirurgie, Québec, Canada;* [3] *CHA Hôpital Saint-Sacrement, Médecine Nucléaire, Québec, Canada;* [4] *Université Laval, Unité de Recherche en Santé des Populations (URESP), Québec, Canada*

Introduction: A reliable method to evaluate sentinel lymph node status intraoperatively would allow to perform sentinel lymph node biopsy and axillary dissection during the same operative time.

Purpose: To evaluate the accuracy of cytologic imprint in assessing sentinel node status intraoperatively.

Patients and Methods: In 380 women with breast cancer, a sentinel lymph node biopsy was attempted at our centre, as part of the NASBP, between July 1998 and August 2001. Sentinel nodes were sectionned in two halves from which cytologic imprints were realized, fixed in ethanol, stained with hematoxylin and eosin and examined intraoperatively. The nodes were then fixed formaline, included in paraffin, sectionned at 6 levels and stained with hematoxylin and eosin. Immunohistochemistry with CAM5.2 was not used routinely, as prescribed by the NSABP protocol. The results for cytologic imprints and definitive histology were correlated using histology as the gold standard. Data were stratified for histologic type of the primary tumor, histologic grade, nuclear grade, and micrometastases (< 0.2 cm) and the differences in the rate of detection were assessed using Fisher's Exact Test.

Results: Cytologic imprints and histology were available for 292 sentinel nodes. The accuracy of intraoperative cytologic imprint was 88.7%. The positive predictive value was 97.9% and the negative predictive value 86.9%. The specificity was 99.5%. The overall sensitivity was 59.0%, but there were significant differences in the rate of detection when the re-

sults were stratified for micrometastases (p=0.00005) and nuclear grade (p=0.0004), but not histologic grade (p=0.15) nor histologic grade (p=0.69).

Conclusion: Cytologic imprint to evaluate sentinel lymph node status intraoperatively has the potential to allow the performance of sentinel node biopsy and axillary dissection during the same operative time in 59% of women who need axillary dissection based on sentinel lymph node positivity, with the remainder receiving axillary dissection subsequently.

Friday, 22 March 2002 16:30–18:00

PROFFERED PAPERS

Treatment of early disease

411 ORAL

Impact of a boost dose of 16 Gy on local control in patients with early stage breast cancer older than 50 years of age

C. Vrieling[1], H. Bartelink[1], L. Collette[2], A. Fourquet[3], J.C. Horiot[4], J.J. Jager[5], M. Pierart[2], P. Poortmans[6], H. Struikmans[7], W. Van den Bogaert[8]. *[1] The Netherlands Cancer Institute, Radiotherapy, Amsterdam, The Netherlands; [2] EORTC, Brussels, Belgium; [3] Institut Curie, Radiotherapy, Paris, France; [4] Centre G.F. Leclerc, Radiotherapy, Dijon, France; [5] RTIL, Radiotherapy, Heerlen, The Netherlands; [6] Bernard Verbeeten Institute, Radiotherapy, Tilburg, The Netherlands; [7] University Hospital, Radiotherapy, Utrecht, The Netherlands; [8] University Hospital Gasthuisberg, Radiotherapy, Leuven, Belgium*

Purpose: To measure the impact of a boost dose of 16 Gy as part of breast conserving therapy, on local control in patients older than 50 years of age.

Patients and Methods: In the EORTC "boost versus no boost" trial, 5569 early stage breast cancer patients underwent tumorectomy followed by whole breast irradiation of 50 Gy. 3692 patient older than 50 years of age, with a microscopically complete excision of the tumor, were randomized between no boost or a 16 Gy boost. A significance level of 0.01 or less was used for subgroup analyses. The median follow-up was 5.1 years.

Results: Patients in the no boost group had a 5-year local recurrence rate of 4.1% (95% CI: 3.1 - 5.1) compared with 3.0% (95% CI: 2.0 - 3.8) for patients in the boost group (p = 0.02). The hazard rate on local recurrence was reduced with a factor of 0.65 (99% CI: 0.40 - 1.04). Multivariate analysis showed that performance status, excision volume and pathological tumor size were significantly related to local control. According to these factors a prognostic score was defined, leading to three different prognostic groups with a 5-year local recurrence rate of 2.5% (95% CI: 1.8 - 3.3), 4.5% (95% CI: 3.2 - 5.8) and 8.6% (95% CI: 4.9 - 12.2), respectively. The influence of the boost on local control was assessed for the different groups separately, but the boost did not improve local control significantly in any of the prognostic groups.

Conclusions: In contrast to the findings in patients younger than 50 years of age [1], the boost did not improve local control significantly for patients with early stage breast cancer older than 50 years of age. Also, no subgroups of patients older than 50 years of age who might significantly benefit from the boost dose could be defined. Although longer follow-up is needed before definite conclusions can be reached, thus far the influence of the boost on local control for patients older than 50 years of age seems limited.

References

[1] Bartelink H, Horiot JC, Poortmans P, Struikmans H, et al. Recurrence rates among women treated with high-dose radiation for early breast cancer. N Eng J Med 2001; 345, 1378-1387

412 ORAL

Breast conserving therapy for early breast cancer. Brachytherapy or photon beam boost: a randomized study

M. Greco[1], L. Lozza[2], S. Tana[2], A.M. Cerrotta[2], G. Gardani[3], R. Kenda[4], M. Gennaro[1], C. Ferraris[1], R. Zucali[5]. *[1] Istituto Nazionale Tumori, Breast Unit, Milan, Italy; [2] Istituto Nazionale Tumori, Radiotherapy, Milan, Italy; [3] Università Bicocca, Milan, Italy; [4] Fondazione Maugeri, Radiotherapy, Pavia, Italy; [5] San Donato Milanese, Radiotherapy, Milan, Italy*

Purpose: The results of breast conserving treatment using breast irradiation and a boost to the tumour bed with either interstitial 192 Iridium implants or photon beam were reviewed.

Materials and Methods: From 1990 to 1994 at the Istituto Nazionale Tumori of Milan 111 patients with T1 or T2 * 2.5 cm breast carcinoma were treated with Tumorectomy, Axillary dissection and breast irradiation (T.A.RT.). The breast was treated with tangential fields using 60 Co or 6 MV photons to deliver 46 Gy in 2 daily doses, in 5 weekly fractions. Patients were randomised to receive a 14 Gy boost with a photon beam (T.A.RT.f: 60 patients) or a brachytherapy implant (T.A.RT.Ir: 51 patients). Radioopaque clips placed by the surgeons in the tumour bed were used to determine the volume to be boosted. High-energy photon beams were used and the dose was given by conventional fractionation in T.A.RT.f group. Patients randomised for T.A.RT.Ir needed a second hospital admission to have a multi or, less frequently monoplanar low dose rate 192 Ir implant performed with after loading technique.

Median follow up was 7 years. We compared occurrence of Ipsilateral Breast Cancer Recurrence (IBCR), to assess local control, and Overall Survival.

Results: No significant difference was observed in terms of IBCR (6.2% vs 6.1% in T.A.RT.f and in T.A.RT.Ir respectively). For tumours up to 1.5 cm the incidence of IBCR was 2.7% in T.A.RT.f and 3.7% in T.A.RT.Ir groups. When tumour was > 1.5 cm, the rate was 9.1% and 4.3% respectively. No local relapses were found in patients up to 55 years old treated with T.A.RT.Ir vs a 6.7% in T.A.RT.f group. The opposite was observed for patients over 55 years (11.1% in T.A.RT.Ir vs no events in T.A.RT.f).

OS was 89.9% in TART f and 94% in TART Ir pts.

Conclusions: Although a small number of patients were included in this trial, after a 7 years median follow up, our results suggest the following. There is no significant difference in local control and overall survival for patients treated with either photon beam or interstitial 192 Ir implant boost.

Photons and brachytherapy to boost the tumour bed are equivalent options and the choice should consider radiation safety and cost.

413 ORAL

The BASO II trial of adjuvant radiotherapy. V. None and tamoxifen. V. None in small, node negative, grade I tumours

R.W. Blamey, U. Chetty, A. Mitchell. *On behalf of the British Association of Surgical Oncology (BASO) Breast Group; Nottingham City Hospital, Nottingham Int. Breast Education Centre, Nottingham, UK*

Tumours (n = 1172) with excellent prognosis (≤2 cm, LN negative, Grade I), age <70, treated by wide local excision (WLE) with histologically clear margins randomised to WLE only, WLE + RT, WLE + Tamoxifen (TAM) or WLE + TAM + RT.

Centres could enter to all 4 arms (or) elect regarding RT and enter the TAM comparison (or) elect regarding TAM and enter the RT comparison.

This analysis is of the first 1122 to follow up date 30 June 2000 (median 35 months, range 1–104). 33 have died: only 7 with or from breast cancer.

	Randomised comparison					
	RT	no RT	TAM	no TAM	RT + TAM	Neither
n	554	549	208	207	96	95
LR	7	20	2	8	0	6
LR% PA	0.4	1.2	0.3	1.3	0	2.1
	χ^2 5.14 p < 0.02		Exact Test p 0.06		Exact Test p 0.01	

Conclusion: In this excellent prognostic group although the LR rate without RT is satisfactory at 1.2% PA, it reaches 2% PA in cases not given neither RT nor TAM.

414 ORAL

Intraoperative radiotherapy in boost modality after breast conserving surgery in breast cancer patients

R. Reitsamer[1], F. Peintinger[3], F. Sedlmayer[2], M. Kopp[2], C. Menzel[1], W. Cimpoca[1], S. Glueck[1], H. Rahim[2], P. Kopp[2], H. Deutschmann[2]. *[1] Landeskliniken Salzburg, Spezielle Gynaekologie, Salzburg, Austria; [2] Landeskliniken Salzburg, Radioonkologie, Salzburg, Austria; [3] Landeskrankenhaus Leoben, Gynaekologische Abteilung, Leoben, Austria*

Introduction: Conventional radiotherapy after breast conserving surgery is confined to 50 to 55 Gy external beam radiation therapy (EBRT) to the whole breast and 10 to 16 Gy external boost radiation to the tumor bed or