

$p < 0.001$ ), and to be seated in central quadrants (53% vs 32%,  $p < 0.001$ ). Other variables were not significantly different. When attempted, IM SN biopsy was successful in 98% of the pts (48/49). There were no major complications, and only two minor bleeding episodes were seen. 24 pts presented with negative SNs both at the IM and axillary basins. 10 pts had a positive axillary SN and a negative IM SN. 10 pts had both positive axillary and IM SNs. 4 pts had a positive IM SN and a negative axillary SN. Altogether, IM SNs were positive in 14 pts (29%).

**Comment:** Using peritumoral injection and preoperative lymphoscintigraphy, IM SNs can be identified in 22% of breast cancer pts. Such pts tend to be relatively young, have central quadrant lesions and display a complex pattern of drainage to SNs (axilla and IM). IM SN biosy is feasible and has low morbidity. Important prognostic information can be derived from such procedure. Also, IM radiotherapy can be offered on a selective basis.

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ORAL

### Elastic scattering spectroscopy for intraoperative detection of sentinel lymph node metastasis

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**Background:** Intra-operative assessment of sentinel lymph node (SLN) enables the surgeon to decide on immediate axillary lymph node dissection at the time of SLN biopsy. The aim is to develop a device using the principles of Elastic Scattering Spectroscopy (ESS) capable of intraoperative detection of SLN metastasis in patients with invasive breast cancer.

**Methods:** ESS involves the spectral analysis of light scattering by intra- and extra-cellular components, and has previously been demonstrated to be sensitive to morphological changes of tissue.

The ESS system consists of a white light source, a parallel pair of optical fibres, a spectrometer and a computer. The process involves the delivery of light from the light source directly onto the sectioned surface of LN via one of the optical fibres. After having been scattered by the tissue, the light is collected by the second optical fibre, and is analysed by the spectrometer and the computer, generating an optical spectrum. The entire process takes less than one second.

The optical spectrum was further analysed against a larger and independent training set of optical spectra from LN using model based analysis to determine the status of LN. The result was compared the histological findings.

**Results:** In total, 75 LN were tested. ESS provided diagnosis in 72 LN (3 LN were deemed indeterminate), and was correct in 62 LN. ESS was able to correctly identify metastasis in 16 out of 19 LN compared with histology. There were 7 false positives and 3 false negatives, thus giving a sensitivity of 84.2% and specificity of 86.8%.

**Conclusion:** Current intra-operative techniques to assess SLN are imprint cytology and fresh frozen section, which are time consuming and operator dependent. ESS has the potential to provide instant and non-operator dependent intra-operative analysis of SLN in patients with breast cancer; sensitivity and specificity should increase as the database of correlated biopsies increase in size.

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ORAL

### Lymphoscintigraphy in breast cancer- which radiopharmaceutical to use- comparison of two particle sizes (ALBU-RES and Nanocoll)

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**Aim:** The aim of the study was to evaluate and compare the visualisation of sentinel nodes in lymphoscintigraphy in breast cancer using two radionuclides.

**Patients and Methods:** The prospective observational study included 269 consecutive patients with clinical stage T1- T2, N0 breast cancer, who underwent lymphatic mapping and sentinel node biopsy using a 2-day protocol. Lymphoscintigraphy was performed four hours after an intratumoral injection of 80-100 MBq 99mTc labelled human albumin colloid with particle size of 0.2-3µm, (ALBU-RES) in 136 patients (group A) or 99mTc albumin microcolloid with particle size of less than 80nm (Nanocoll) in 133 patients (group N) in a volume of 0,2ml. Anterior and lateral views were obtained

using a gamma camera. The intensity of uptake in the nodes was classified as weak, clear, strong or absent.

**Results:** The lymphoscintigraphy showed sentinel nodes in the axilla in 114 of 136 patients (84%) in group A. The median number of the visualised nodes in the axilla was 1 (range 1- 4) in these 114 patients. In group N, 118 of 113 patients (89%) had a median of 2 (range 1-5) hot spots in the axilla ( $p < 0.0005$  for the median number of visualised nodes between the patient groups. The proportion with clear or strong uptake of the tracer in the axilla was 66% in group A and 79% in group N ( $p < 0.05$ ). Sentinel lymph nodes in the internal mammary basin were visualised in 18 (13%) patients in group A and in 27 (20%) in group N ( $p = ns$ ).

**Conclusion:** More numerous and intense hot spots were visualised in the axilla when using smaller particle size (Nanocoll) pharmaceutical.

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POSTERS

## Sentinel node – technique, diagnosis and management

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POSTER

### Sentinel node biopsy using small-sized Tc-99m Tin colloid

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**Objective:** The optimum particle size of pharmaceuticals for sentinel lymph node biopsy (SLNB) is still one of the major problems in SLNB. Small-sized particles move easily, but also pass through the SLNs rapidly. On the contrary, large particles move slowly to the SLNs, but stay there for longer. We produced small-sized tin colloid particles and evaluated the clinical usefulness of these particles.

**Patients and Method:** Patients with no axillary lymph node swelling were recruited to this trial. We produced small-sized tin colloid particles (200-400 nm) by mixing sodium pertechnetium-99m and SnCl<sub>2</sub> at the ratio of 1:4, instead of the usual 1:1 ratio. SLNB was performed by injecting 0.5 ml of 74 MBq/ml of this solution at three points peritumorally and 0.2 ml subcutaneously just over the tumor the day before the operation. Isosulfan blue was also injected peritumorally just before the operation. SLNB was performed using a gamma probe, and a back-up dissection was also performed.

**Results:** SLNB using the small-sized Tc-Tin colloid particles was performed in 50 patients (SC group). Seventy-four patients in whom the biopsy was performed using large-sized tin colloid particles were examined as controls (LC group). The number of SLN identified and the identification rate were 1.9 and 79% in the LC group, and 3.3 and 100% in the SC group, respectively. The false-negativity rate was 9.6% and 5%, respectively, in the two groups.

**Conclusion:** Small-sized Tc-99m tin colloid particles are more useful for SLNB as compared to large- sized tin colloid particles.

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POSTER

### Ultrasound guided fna of the axillary lymphnode: a preoperative staging procedure in primary breast cancer

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Currently, the axillary lymphnode dissection is being replaced by the sentinel node procedure. This method is time-consuming and the full immunohistochemical evaluation is often first known post-operatively. This study was designed to evaluate the accuracy of pre-operatively ultrasound guided fine needle aspirations (FNA's) for the detection of non-palpable lymph node metastases in primary breast cancer patients.

**Material and Methods:** We evaluated the material of 183 ultrasound guided FNA's of non-palpable axillary lymph nodes of primary breast cancer patients. The cytological results were compared with the final histological diagnosis and analyzed with descriptive statistical methods.

**Results:** Of the total of 85 patients with histologically proven lymph node metastases, 37(44%) were cytologically detected. A clear relation between the number of positive nodes, tumor size and cytological detection was observed since 83% of the group of tumors with more than 3 positive nodes was cytologically detected, of which 54% were T2 tumors. In addition 25% of the cytologically false negative nodes were found to contain micrometastases only.

**Conclusion:** Ultrasound guided FNA of the axillary lymph node is a simple method, that should be included in the preoperative staging procedure of primary breast cancer patients to select those who need a complete axillary lymph node dissection at primary surgery.

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POSTER

### The role of dynamic imaging in sentinel lymph node biopsy in breast cancer

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**Introduction and Aim:** The use of radiopharmaceutical in sentinel lymph node (SLN) biopsy enables preoperative visualisation of SLN. However, the precise role of preoperative imaging remains undefined in SLN biopsy for breast cancer. Furthermore, there has been no published study to date in evaluating the role of dynamic imaging. The aim of this study is to evaluate the role of high resolution, early dynamic imaging in SLN biopsy for breast cancer, primarily through direct visualisation and analysis of radiopharmaceutical transit through lymphatic tracts.

**Methods:** Patients with T1/T2, N0 invasive breast cancer underwent SLN localisation using intra-dermal injection of 15 MBq of 99mTc-nanocolloid. Gamma camera anterior-oblique dynamic imaging commenced simultaneously with tracer administration for 45 minutes, and was followed by anterior and lateral static imaging. Dynamic imaging data was reformatted into image files of different time frames. Patterns of uptake were analysed using the sequences of dynamic frames and time activity curve.

**Results:** SLN localisation was successful in 70/73 studies (95.9%) in 72 patients. Imaging information was present within the first 15 minutes of dynamic imaging in 67/70 studies (95.7%). Critical analysis of dynamic data helped to differentiate true SLN from secondary echelon nodes in 8 studies and transient foci of radioactivity in 6 studies. In 17 studies, SLN contained metastatic disease. The detection of SLN metastasis was independent from the use of dynamic imaging.

**Conclusion:** Dynamic imaging improves the interpretation of preoperative SLN imaging for breast cancer, but does not contribute significantly to the successful detection of SLN. Hence preoperative dynamic imaging is not necessary in SLN biopsy for breast cancer.

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POSTER

### Causes of false-negative result in sentinel node biopsy using radiocolloid in patients with breast cancer

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**Introduction:** False-negative result is a major problem in sentinel node (SN) biopsy for patient with breast cancer. The purpose of this study is to discern the mechanism of incorrect positive SN identification based on our results of SN biopsy using radiocolloid.

**Material and Methods:** From April 1999 through September 2001, 203 patients underwent SN biopsy using Tc-99m rhenium colloid. One day before surgery, 0.2-0.4 ml (74 to 185 MBq) of rhenium colloid was injected into breast tissue surrounding the tumor. Lymphoscintigraphy was performed 2 hours after injection; SN biopsy was performed 20 hours after injection. Identification of SN was by gamma probe for hot SN or with intraoperative axillary palpation for "hard and cold" SN. Routine HE and immunohistochemical staining at 2 mm intervals was used to analyze SN.

**Results:** Hot SN was identified in all patients. The "hard and cold" SN was harvested additionally in 8 patients; these "hard and cold" SNs were fully invaded by cancer cells. SN was positive in 79 patients. In 63 of 124 patients with negative SN, axillary lymph node dissection was performed. There was no false-negative result. In 61 (77.2%) of 79 patients with positive SN, metastasis was seen in the hottest SN. In 15 (19%) patients, metastasis was seen solely in a hot, but not the hottest, SN. In 6 of these 15 patients, radioactivity of positive node was less than 20% of hottest SN radioactivity. In 11 of the 15 patients, positive SN was located at the tumor side of hottest SN. In 3 (3.8%) patients, only the "hard and cold" SN was positive.

**Conclusion:** This study suggests that overlooking of positive non-hottest SN with faint radioactivity and failure to detect "hard and cold" SN are the main causes of false-negative result in SN biopsy using radiocolloid.

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POSTER

### Radioguided surgery of non-palpable breast lesions (NPBL)

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The aim of this study was to determine the feasibility of the radioguided occult lesion localization (ROLL) technique for the excision of NPBL and, in the case of malignancy, for sentinel lymph node biopsy (SLNB). From October 2000 to September 2001, 92 patients with NPBL underwent ROLL procedure. Injection of 20-80 MBq 200-600 nm particle sized colloid in 0.4 ml volume into the lesion under ultrasound (56 patients) or mammography (36 patients) guidance was performed in the afternoon prior to surgery. There were 64 mass lesions and 28 microcalcifications. Lymphoscintigraphy was performed in the morning of the day of surgery on the 48 patients on whom SLNB was also planned. Patent blue dye (2 ml) was injected subareolarly before surgery. Gamma-probe was used for intraoperative localization. Specimen radiography was done in all cases. The excision of the lesion was successfully performed in 91 patients (99%). In 4 cases no drainage was detected on lymphoscintigraphy, and no sentinel lymph node could be localized and removed during surgery. Success rate for SLNB was 92%. Image guided intralesional radiotracer administration is feasible for localizing non-palpable breast lesions and also allows SLNB.

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POSTER

### Is a quality control feasible in daily practice of sentinel lymph node (SLN)?

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The only quality test of good practice of SLN (i.e. identification of the "true" SLN) is the assessment of false-negative rate. Of course, it is impossible when the SLN procedure become a standard procedure without complete axillary dissection (CAD) if SLN is negative. So, we propose a regular comparison of results of SLN with a data system reporting macroscopic tumor size (pT) and positive node risk.

**Methods:** One of the authors retrospectively establish this data system with 893 patients with invasive breast cancer and CAD. The rate of positive node is 11.1% for pT= 0 to 9.9mm; 17.7% for pT=10 to 14.9mm; 26.5% for pT= 15 to 19.9mm; 30.1% for pT=20 to 24.9mm; 36% for pT=25 to 29.9mm. This current study prospectively compare with this data, 100 patients with invasive breast cancer, treated between 01/02/01 and 31/08/01 and in which SLN were mapped. All patients are T0,T1, N0,M0, with unifocal tumor and no prior treatment. SLN procedure use combined technic (technetium-labeled sulfur colloid and blue patent) with peritumoral or subareolar (non-palpable lesion) injection. A positive SLN is defined as any SLN positive when examined with routine hematoxylin and eosine and safran (HES) stains or immunohistochemical (IHC) stains for cytokeratin. Any positive SLN (HES or IHC) have a CAD.

**Results:** Detection rates is 96%. The 4 patients without detected SLN have CAD, 3 are N+. 25 SLN are positive: 14 metastasis HES, 3 micrometastasis HES, 8 micrometastasis IHC. In relation with pT in the data system, the expected number of patients N+ is 18 to 20 and the found number of N+ is 28, this result (found N+ > expected N+) is related for all size interval

**Conclusions:** We think it is necessary to assess the results of SLN procedure in relation with a data system. If appear discordance, any procedure stage must be checked to determine failure reason.

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POSTER

### Motion restriction and the axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer

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**Background:** Axillary web syndrome (AWS) is a self-limiting cause of morbidity in the early postoperative period after axillary surgery first described by Moskovitz and coworkers 2001. Pain and limited range of motion associated with palpable cords of tissue in the axilla are typical symptoms and signs for AWS. The proposed pathogenesis is lymphovenous injury, stasis and hypercoagulability caused by axillary surgery.

**Aim:** The aim of this prospective study was to evaluate the rate and causes of motion restriction, and especially the incidence of AWS after sentinel node biopsy (SNB) and axillary clearance (AC).

**Patients and Methods:** Altogether 85 breast cancer patients who underwent SNB only (49 patients, the SNB group) or SNB and AC (36 patients, the AC group) were examined before surgery and two weeks and three months after the operation by a physiotherapist. The range of shoulder flexion and abduction were measured and the reasons for limited movement were registered. The presence and extent of AWS were evaluated by inspection and palpation of the axilla and the arm.

**Results:** At two weeks after surgery, the range of shoulder abduction and/or flexion was restricted in 24 (45%) patients after SNB only and in 31 (86%) patients who also underwent AC ( $p=0.002$ ). AWS was encountered in 10 (20%) patients with SNB and 26 (72%) with AC ( $p<0.00005$ ). AWS was the most common reason for limited range of motion in the AC group. The other reasons for restricted shoulder abduction and flexion were pain or strain in the wound, the pectoral muscles and/or in the axilla. Three months after surgery, a recovery with full range of motion and resolution of AWS was observed in all patients except one in both patient groups.

**Conclusions:** In the SNB group, a more rapid recovery with significantly less postoperative morbidity was observed compared to AC. In the AC group, AWS is a significant cause for early postoperative morbidity.

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POSTER

### Sentinel node biopsy in breast cancer: comparison between tin colloid and stannous phytate

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**Background:** Recently sentinel node biopsy has been introduced as an accurate staging method for breast cancer. However the choice of radioactive tracer is still controversial. This study used technetium-99m stannous phytate (Dai-ichi Radioisotope, estimated particle size of 200-1000nm) and technetium-99m tin colloid (Nihon Medi-Physics, particle size 400-5000 nm). Both of them are commercially available in Japan. Tracers such as sulfur colloid and colloidal albumin, popularly used in western countries, has not been available in Japan. The aim of this study is to compare these two agents and to find out optimal tracer.

**Materials and Methods:** 85 patients with breast cancer, no clinical evidence of axillary metastasis (T1N0M0, T<3 cm), were studied. Tin colloid (43 patients) and stannous phytate (45 patients) were used as radioactive tracers. On the day of operation 1ml (37 MBq) radioactive agent was injected subdermally over the primary tumor. Lymphoscintigraphy, anterior and anterior-oblique projection, was performed from 15 min to 4 hours after the injection. Surgery was performed from 1 to 5 hours after the injection. A hand-held gamma probe guided sentinel node biopsy was performed. A node with more than 10% of the hottest nodal activity was defined as a sentinel node.

**Result:** Identification rate by lymphoscintigraphy was 67% with tin colloid and 98% with stannous phytate, respectively. Over all identification rate during operation was 88% with tin colloid and 98% with stannous phytate respectively. The number of sentinel nodes collected per patient was 1.5 with tin colloid and 1.7 with stannous phytate respectively. No internal mammary sentinel node was detected in both groups.

**Conclusion:** This study suggests that technetium-99m stannous phytate may be superior to technetium-99m tin colloid for lymphatic mapping.

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POSTER

### Touch imprint cytology in the assessment of sentinel lymph node status

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**Aim:** The aim here was to study the usefulness of touch imprint cytology in the intraoperative assessment of the sentinel lymph node status in patients with breast cancer.

**Materials & Methods:** Sentinel lymph node (SLN) biopsy was performed in breast cancer patients undergoing surgery using the isotope and / or blue dye. This was followed by a standard level II axillary clearance and removal of the primary tumour by wide excision or mastectomy. Touch imprint slides were taken from the bisected SLN and stained with both conventional and immunohistochemical stains. SLN, other axillary nodes and the primary tumour were sent for routine H & E histological analysis.

**Results:** Over a period of 18 months, 142 patients underwent SLN biopsy. Three patients were excluded as the final histology was non-invasive tumour (DCIS) and the SLN was not identified in 6, leaving 133 patients for analysis.

In 38 patients the SLN and the imprint cytology were both positive for tumour and in 88 patients both were negative. In 4 patients the SLN was positive but the cytology was negative (false negatives). In 3 patients the SLN was negative but the imprint was reported as positive (false positives).

There were 8 false negative sentinel nodes (the SLN was negative but the rest of the axilla was positive). Thus the usefulness of the touch imprint cytology in predicting the axillary lymph node status as a whole was as follows;

In 38 patients the axilla was positive and the imprint was also positive. In 80 patients the axilla and the imprint were both negative. In 12 patients the axilla was positive but the imprint was negative (false negatives). In 3 patients the axilla was negative but the imprint was positive.

The results indicate that out of 133 patients, 118 (89%) had the correct axillary nodal status predicted by touch imprint cytology. Only 12 patients (9%) would have been recalled for further surgery (axillary clearance) and 3 patients (2% of the total) would have had a potentially unnecessary axillary clearance.

**Conclusions:** Touch imprint cytology appears to be a useful technique in the intraoperative assessment of the sentinel node status and may help to avoid a second operation in the majority of patients with a positive axilla.

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POSTER

### Combination technique with dye and radiolabelled tin colloid is superior to dye alone in identification of the sentinel node in breast cancer

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**Background:** The purpose of the present study was to evaluate whether the combination of dye and radioisotope would improve the detection rate of sentinel nodes (SN) and the diagnostic accuracy of axillary lymph node status over dye alone in patients with breast cancer.

**Methods:** Sentinel node biopsy (SNB) was performed in Stages or breast cancer patients with clinically negative nodes using dye alone (indocyanine green) or a combination of dye and radioisotope (99mTc-radiolabelled tin colloid).

**Results:** SNB guided by dye alone was performed in 192 patients and SNB guided by a combination of dye and radioisotope was performed in 194 patients. The detection rate of SN was significantly ( $P>0.0001$ ) higher in the combination group (96%) than in the dye alone group (74%). The sensitivity, specificity, and overall accuracy of SNB in the diagnosis of axillary lymph node status were 96.5, 100, and 99%, respectively, for the combination group, and 83, 96.5, and 94.9%, respectively, for the dye alone group. There were two (3.5%) false negatives in the combination group, but seven (17%) false negatives in the dye alone group. The combination method was significantly superior to the dye alone method for sensitivity ( $P=0.03$ ) and accuracy ( $P=0.04$ ).

**Conclusions:** The addition of a radioisotope to the dye in SNB increases detection rate of SNs in breast cancer patients, and SNs detected by the combination method predict the axillary lymph node status with greater accuracy than those detected by the dye alone method.

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POSTER

### Axillary lymph node mapping by using 3-dimensional magnetic resonance imaging and novel surgical sampling for assessment of nodal status in breast cancer

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**Background:** We have reported that magnetic resonance imaging (MRI) is the best method for assessing lymph node size and representing the relation of the lymph node to normal anatomy.

**Methods:** The four largest nodes oriented by 3dimensional MRI (3D-MRI) were sampled in 124 consecutive patients with breast cancer undergoing axillary clearance. Axillary clearance yielded a mean of 16.0 nodes.

**Results:** A method of preliminary sampling of four nodes in the axilla oriented by 3D-MRI was assessed in all cases, 43 of whom were histologically node positive. Based on sampled nodes, of the node-positive patients, lymph node metastases were detected in 40 of 43 (93%). Based on sampled nodes, of the 39 patients with macrometastatic nodes, lymph node metastases were detected in 38 (97%), but only in 2 of the 4 (50%) patients with only one micrometastatic node.

**Conclusions:** This experience indicates that the four largest nodes sampling oriented by 3D-MRI accurately identifies the patients with macrometastatic nodes. This result may be as good as that of surgical sampling reported by the most skilful surgeons.

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POSTER

### Does the procedure for Sentinel lymphadenectomy release tumour cells in the blood of breast cancer patients?

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Sentinel lymphadenectomy (SLND) is now becoming a useful procedure to distinguish breast cancer patients who may not benefit from axillary lymphadenectomy from those in whom complete axillary staging may be necessary. There are two procedures for SLND; dye technique and radio- guided technique. Especially, the dye method requires the procedure "squeezing" of dye-injected breast with tumor, however, the squeezing may have a risk to spread tumor cells into blood stream. In the present study we examined mRNA expression of mammaglobin and carcino- embryonic antigen (CEA) in peripheral blood samples in human breast cancer patients.

Peripheral blood samples were obtained from 17 breast cancer patients at two time points; before and after squeezing for SLND during operations. Mononuclear cells were isolated by gradient-density method and total cellular RNA was extracted to synthesize cDNA by reverse- transcription using an oligo (dT) primer and reverse transcriptase (Superscript II, GIBCO BRL). Quantitative PCR using a TaqMan (Applied Biosystems 7700) was carried out to compare the expression levels of mammaglobin and CEA mRNA by standardizing with GAPDH mRNA expression.

Mammaglobin and CEA mRNA expression was detected in 3 peripheral blood samples before SLND (17.6%), however, no mammaglobin mRNA expression was detected in the rest 14 cases both before and after SLND. No CEA mRNA was expressed in the samples obtained after SLND from cases in whom CEA mRNA was not detected before SLND. Expression of CEA mRNA was detected in only one case before and after SLND (5.9%). Our results suggest that breast cancer cells may exist in the blood before operation in some patients, and that the possibility of tumor cell release after SLND seems to be rare.

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POSTER

### Sentinel lymph node biopsy in breast cancer: our experience with 364 selected patients

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From November 1997 until August 2001, 364 patients underwent in our Center a sentinel lymph node biopsy followed by a complete axillary lymph nodes dissection. All patients had invasive breast cancer in early stage (T0N0 = 66, T1N0 = 131, T2N0 = 81, T0N1A = 1, T1N1A = 12, T2N1A = 13 - T2 < 3 cm f). The injection protocol was 8 mCi peritumoral intramammary or 2 mCi intradermal or a combination of both. The mean number of S.L.N. removed was 3 (1 to 7) and the total axillary lymph nodes 19.

Some patients (<2%) with a S.L.N. non identified were excluded from the study. The percentage of false negatives (F.N.) was 3,57% based on the total number of patients (13/364) or 8,96% for the patients with lymph nodes metastases (13/147).

We had a sensitivity of 91% and a N.P.V. of 94%. If we selected the patients only with a tumor in a stage T0N0 and T1N0 with a S.L.N. mapped after an intramammary injection, the false negative cases were near to zero (1/206, F.N. = 0,48%).

Today, we can propose to our patients the lymphatic mapping only and S.L.N. biopsy followed, if it is necessary, by a complete lymph nodes dissection.

Since, we have already done 92 patients and only 14 out of these (15%) had a positif sentinel lymph node. For the patients with an early invasive breast cancer, the S.L.N. node biopsy is certainly the best surgical treatment at this moment.

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POSTER

### Sentinel lymph node biopsy: experience of the Deschenes-Fabia centre for breast disease

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**Introduction:** Axillary lymph node status is the most important prognostic factor in breast cancer. The morbidity of axillary dissection, the method of choice for assessing axillary lymph node status, calls for an equally accurate but less invasive technique. Sentinel lymph node biopsy is regarded as a promising technique in this regard.

**Purpose:** To evaluate the accuracy of the sentinel lymph node biopsy compared to axillary dissection in our centre.

**Patients and Methods:** In 380 women with breast cancer, a sentinel lymph node biopsy was attempted in our centre as part of the NSABP, between July 1998 and August 2001. Sentinel nodes were sectioned in two halves, fixed in formaline, included in paraffin, sectioned at 6 levels and stained with hematoxylin and eosin. The nodes recovered from axillary dissections were examined at only one level. Immunohistochemistry with CAM5.2 was not used routinely, as prescribed by the NSABP protocol. The results for sentinel and other axillary nodes were correlated.

**Results:** A total of 383 sentinel lymph node biopsies were attempted (3 bilateral cases) and successful in 362 cases (successful procedure rate of 94.5%) of which 103 (28.5%) contained metastases. A total of 208 axillary dissections containing in average 13 lymph nodes (5 to 40 nodes) were realized. In 190 cases, both a successful sentinel lymph node biopsy and an axillary dissection were performed. Sentinel lymph node status and axillary lymph node status (including the sentinel node) were identical in 187/190 cases (accuracy 98.4%). The sentinel lymph node was the only positive node in 55/105 positive cases (52.4%). The negative predictive value was 96.6%. Reserving axillary dissection to women with a positive sentinel lymph node would have reduced the number of axillary dissections from 190 to 102 (46.3%), with only 3 of 88 (3.4%) patients not receiving dissection with node metastases.

**Conclusion:** Sentinel lymph node status is an excellent predictor of axillary lymph node status. After a period of training and validation by axillary dissection, the sentinel lymph node biopsy technique has the potential to reduce by half the number of axillary dissections, with acceptable safety.

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POSTER

**Can sentinel node biopsy improve prognostic discrimination**

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SLNB appears to offer nothing over clearance for assessment of lymph node status but offers an alternative for samplers; however one recent study failed to show advantage over 4 node sampling<sup>(1)</sup>.

The demonstration of micrometastases may lie in the number of sections which if used without SLNB would also raise the detection rate; furthermore micrometastases in LN's do not appear to be of prognostic significance.

There are no assessments of the value of SLNB in improving overall prognostic discrimination. For this LN status has to be used in combination with other factors (eg) grade, size, hormone receptor and SLNB can at best offer only a small advance in prognostic discrimination.

**References**

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POSTER

**Sentinel node biopsy (SNB) for impalpable screen-detected invasive breast carcinoma**

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**Introduction:** SNB has the potential to decrease the axillary morbidity for women with invasive breast carcinoma. For screen-detected invasive tumours, identifying the site for injection of the dye for SNB can be extremely difficult even with a localization wire in-situ. This prospective study demonstrates our results of a simple technique to aid dye placement for impalpable invasive breast carcinomas.

**Method:** Forty-one patients with an impalpable screen-detected carcinoma were selected for needle localised WLE, SNB and completion level I axillary clearance. Stereotactic core biopsy had confirmed the presence of invasion. In theatre, a 20G hollow cannula (Medi plus MED8033) was threaded over the localization guide-wire (Hawkins 2 or 3), allowing the floppy wire to be palpated percutaneously. Injection with Patent Blue V was then performed by direct palpation of the tumour site.

**Results:** A sentinel node (SN) was identified in 35 patients (85%) using blue dye alone. In total, 52 SN were identified (mean = 1.5/patient). Mean node yield following level I clearance was 8.2 (range 3-18). In 28 patients (80%) the axilla was not involved. Seven patients had lymph node metastases; the SN was involved in each patient (0% false negative) and was the only positive node in 6 of the 7 patients.

**Conclusion:** The use of a hollow needle over a stereotactically placed guide-wire allows accurate injection of Patent Blue around screen-detected invasive breast tumours. SNB for impalpable invasive carcinoma appears to be an accurate technique for staging the axilla and needs further assessment.

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POSTER

**Sentinel lymph node biopsy in breast cancer: importance of the internal mammary chain**D. Noterman<sup>1</sup>, P. Bourgeois<sup>2</sup>, D. Hertens<sup>1</sup>, I. Veys<sup>1</sup>, D. Larsimont<sup>3</sup>, J.-M. Nogaret<sup>1</sup>, <sup>1</sup> Jules Bordet - Centre Des Tumeurs De L'université, Surgery, Brussels, Belgium; <sup>2</sup> Jules Bordet - Centre Des Tumeurs De L'université L, Nuclear Medicine Physician, Brussels, Belgium; <sup>3</sup> Jules Bordet - Centre Des Tumeurs De L'université L, Pathologist, Brussels, Belgium

The advent of lymphatic mapping using radiolabelled tracer has permitted to detect extra-axillary drainage in 32% of the first 338 patients investigated in our Center.

From January 2000 until Augustus 2001, we decided to perform biopsy of some internal mammary sentinel lymph nodes. 23 Patients underwent such biopsy. All patients had invasive breast cancer in early stage (T0N0: 4; T1N0: 14; T2N0: 5). They underwent a 8 mCi peritumoral intramammary injection.

The tumour was internal (16), medial (5) or external (2).

Internal mammary sentinel nodes were identified in association with axillary nodes in 18 cases and were exclusive in 5 cases.

The biopsy failed in 7 cases (1 pneumothorax, 1 hemorrhage, 5 technical difficulties).

We found an internal mammary metastasis in 25% of patients (4 cases). It was the only site of metastasis in one case.

We had complications in 2 cases: 1 pneumothorax and 1 hemorrhage. The impact of the internal mammary chain in the treatment of breast cancer has been studied for many years. Whether the internal mammary nodes should be treated locally is controversial.

We can suggest that the biopsy of these nodes may provide a more accurate staging of the disease and a positive impact on the treatment and the outcome of the patients.

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POSTER

**Definition of sentinel lymph nodes in breast cancer using radioisotope and invention of a new gamma probe (Mediprobe)**K. Sato<sup>1</sup>, K. Tamaki<sup>1</sup>, H. Hiraide<sup>2</sup>, H. Mochizuki<sup>1</sup>. <sup>1</sup> National Defense Medical College, Surgery I, Saitama, Japan; <sup>2</sup> National Defense Medical College, Research Institute, Saitama, Japan

**Objective:** The large particles of radiotracer, Tc-tin colloids, have been used for identifying SLNs in breast cancer at our institute since May '97. Here, we tried to make the definition of SLNs concerning the clinical and technical factors, and a handy gamma probe based on the definition was invented.

**Methods:** Detection of SLN was tried in 135 breast cancer patients (T1-2, N0). Two hours prior to surgery, 1 or 3 ml Tc tin colloids (74MBq/ml), was injected peritumorally ( $\pm$ subdermally). The hot spots identified with a gamma probe (Navigator) were regarded as SLNs, and the radioactivity was measured. Patients were divided in high uptake ( $\geq 100$  cps) and low uptake ( $< 99$  cps) groups. The clinical and technical factors affecting the uptake of radiocolloid were examined, and the definition of SLNs was made.

**Results:** SLNs (average 1.6) were successfully identified in 133 patients, consisted of 41 low (35.4cps) and 92 high uptake patients (972.6cps). In multivariate analysis among the clinical factors and technical factors (injection site, volume of injected colloid), the older patients ( $\geq 65$  yrs) and obese (BMI $\geq 25$ ) patients were revealed to be significant independent predictors of low uptake ( $P < 0.05$ ). The radioactivity varies depending on patients, and the threshold for defining SLNs could not be presented.

However, if a hot node showing "a 10:1 ex vivo gamma probe ratio to background" was defined as SLN, all hot nodes could be SLNs. Based on the definition, a handy gamma probe (200g, 2x20cm), "Mediprobe", was invented, which had neither cord nor box, and provided reliable detection of SLNs in four patients.

**Conclusions:** Although further testing on larger samples is required, this small device is promising for easy detection of SLNs.

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POSTER

**Sentinel node biopsy (SNB): use of intraoperative cytology to decide on synchronous axillary lymph node dissection (AD) and primary lesion surgery**M. Llatjós<sup>1</sup>, E. Castellà<sup>1</sup>, M. Fraile<sup>2</sup>, M. Rull<sup>3</sup>, F.J. Julián<sup>3</sup>, F. Fusté<sup>4</sup>, V. Vallejos<sup>2</sup>, A. Barnadas<sup>5</sup>, R. Penin<sup>1</sup>, A. Casals<sup>1</sup>. <sup>1</sup> Hosp. Germans Trias I Pujol, Pathology, Badalona- Barcelona, Spain; <sup>2</sup> Hosp. Germans Trias I Pujol, Nuclear Medicine, Badalona- Barcelona, Spain; <sup>3</sup> Germans Trias I Pujol, Surgery, Badalona- Barcelona, Spain; <sup>4</sup> Germans Trias I Pujol, Gynaecology, Badalona- Barcelona, Spain; <sup>5</sup> Germans Trias I Pujol, Oncology, Badalona-Barcelona, Spain

SNB is an alternative to AD. After validation (November 1999 at our centre), the goal of SNB is to spare AD in pN0 pts. Given that positive SN pts must receive AD, a second surgical procedure will always be needed unless intraoperative assessment is at hand. We report on the use of cytology to decide on synchronous AD and primary lesion treatment.

**Patients and Methods:** From December 1999 through September 2001, 109 T $\leq$  3 cm, N0 patients underwent SNB at our institution. Peritumoural injections of Tc-99m albumin colloid, lymphoscintigraphy and a gamma probe were used. SNB was done in the first place. SN was sent for fresh processing while the surgeon proceeded with the primary. SNs were sectioned at 2 mm intervals. Air-dried smears were obtained by scraping the cut surfaces (2 to 6). Smears were stained with a rapid Giemsa method and examined by an experienced cytopathologist. The intraoperative analysis took less than 15 minutes. Definitive histology included serial sectioning and staining with both H&E and cytokeratin. Assessment was done by an independent pathologist.

**Results:** Patient age was 36 to 83 years (mean 55). Tumour size was 0.4 to 3 cm (mean 1.6 cm). The mean number of SNs was 1.6. Of the 109

patients, 32 showed a positive SN at intraoperative cytology. There were no false positive cases. 77 patients were negative for cytology. 14 of them (18%) were converted to positive after detection of micrometastases (< 2 mm) on definitive histology. No macrometastases were missed. Altogether, the decision to perform (n = 32) or not to perform AD(n = 63) was correct in 87% of patients. A second operative procedure was avoided in 32 of the 46 positive cases (70%).

**Comment:** Intraoperative assessment of the SN using imprint cytology allows for relevant decision-making concerning synchronous AD and primary lesion excision. Only the minority of patients with micrometastases in the SN are likely to need a second surgical procedure. Such approach is convenient both for patient comfort and cost-containment.

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POSTER

### Sentinel node biopsy (SNB) and the accuracy of intra-operative imprint cytology (IC)

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Sentinel lymph node biopsy (SNB) has the potential to decrease axillary morbidity for women with node negative invasive breast cancer. The diagnosis of metastases in sentinel nodes however is usually made after surgery. Frozen section of the sentinel node has been performed intra-operatively but is still unreliable. The aim of this study was to investigate whether imprint cytology (IC) of sentinel lymph nodes was feasible and accurate.

Women suitable for SNB were entered into the study from the audit phase of the ALMANAC trial. SNB was performed according to the trial protocol. All sentinel nodes excised were submitted fresh to the pathologist for assessment. Following SNB, each patient underwent completion axillary clearance. Each sentinel node was bisected and an imprint taken from the fresh lymph node. All nodes were then fixed and processed. The final histology of the sentinel nodes was compared to the imprint cytology.

Fourteen patients have so far been enrolled into the study in whom a total of 32 sentinel nodes were identified and submitted for imprint cytology (mean, 2.3/patient). Six patients (43%) had lymph node metastases (8 nodes); the sentinel node was involved in 5 patients (16% false negative). The sensitivity for all sentinel nodes for IC was 50% (4/8 nodes) but was 80% for IC for the number of patients identified with a positive axillary node (4/5 patients). This was because one patient with 4 positive sentinel nodes only had one node positive for IC. However, specificity for IC was 100% (24/24 nodes). There were no false positive results for IC (PPV 100%), and negative predictive value was 86% (24/28).

The use of IC intra-operatively may allow the identification of positive sentinel nodes in the majority of patients, thus allowing definitive axillary surgery in the majority of patients in whom it is indicated.

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POSTER

### Patient preference for dissection of sentinel nodes outside the axilla

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**Background:** Lymphoscintigraphy with biopsy of sentinel nodes outside the axilla may provide a promising method providing information of the complete lymphatic drainage of the tumour area in breast cancer. The procedure seems not to carry considerable risks for patients, but an additional skin incision is necessary in connection with breast conserving surgery and lateral tumour location. However, the role of biopsy of sentinel nodes outside the axilla in staging of breast cancer is still obscure.

**Aim:** We aimed to evaluate the patients' and female doctors' opinions about harvesting sentinel nodes outside the axilla and study the patients' ability to understand the concept of sentinel node biopsy.

**Patients and Methods:** An information leaflet and a questionnaire was mailed to 100 consecutive breast cancer patients who had undergone sentinel node biopsy and to 300 female doctors. Patients older than 75 years and those with sentinel nodes outside the axilla in the lymphoscintigraphy were not included.

**Results:** Seventy-three (73%) patients and 148 (49%) female doctors returned the questionnaire. Fifty-eight (79%) breast cancer patients and 71 (48%) female doctors wanted harvesting of sentinel nodes outside the axilla just to know if those nodes were involved. Sixty-six (90%) patients and 128 (86%) doctors wanted the procedure if there were even a slightest prob-

ability (10% or less) that it would change adjuvant treatment. Sixty (82%) patients had understood if the sentinel node in the axilla was found in their case.

**Conclusion:** Breast cancer patients seem to appreciate the information gained by harvesting sentinel nodes outside the axilla and want the procedure if there is even a slightest possibility that it may change the adjuvant treatment.

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POSTER

### Targeting the true sentinel node: the contribution of the subareolar plexus concept

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**Introduction:** Several studies have been published supporting the use of a combined technique for a proper Sentinel Node (SN) mapping and biopsy. However, there are a wide variety of "combined" techniques. The Sappey's subareolar lymphatic plexus, being the place where the the whole breast lymph flow reunites before heading to the axilla, can be used to the isotope and/or dye injection.

**Methods:** We studied a series of 92 consecutive patients with cN0 breast cancer, submitted to the SN procedure, from Jul/99 to Jan/01. We used a combination technique, with peritumoral Tc99m sulphur colloid injection (1mCi), subareolar Patent blue V dye (0.5-1 cc) injection and hand-held gamma-probe detection. All patients received a standard level 1-2 axillary dissection. Statistical significance was assessed using Chi-Square test (SPSS 8.0).

**Results:** All patients were females. The median of age was 58.5 years (24-88). The median of tumour size was 23.5 mm (1-70). There were 2.2% of pT1a, 5.4% of pT1b, 25.0% of pT1c, 60.9% of pT2 and 6.5% of pT3. We performed 68.5% of modified radical mastectomy and 29.3% of conservative surgery. The median of axillary nodes was 16.5 (5-38).

The SN identification rate was 98.9% (91/92). The median number of SN was 1 (0-4). Forty-five percent (41/92) of the patients were pN+. Sentinel node was the only positive node in 46.3% (19/41). The false-negative rate was 7.5% (3/40). The overall accuracy was 96.7%. Lymphoscintigraphy was negative in 5.4% of cases (5/92). The SN were hot and blue in 78%, only blue in 15.4% and only hot in 6.6%; 84.6% were hot and 93.4% were blue (p<0.001).

**Conclusions:** This combined technique allows an excellent identification rate with an acceptable false-negative rate. The easy and reproducible subareolar dye injection can make the difference in case of negative lymphoscintigraphy, nonpalpable or previously excised tumours.

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POSTER

### Sentinel node biopsy: learning, validating and introducing as standard of care

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The optimal technique of sentinel node biopsy (SNB) is still debated. We compare two methods of SNB, describe our learning phase, the validation of the methods and the first results after implementing SNB as standard of care in selected breast cancer patients.

SNB with peritumoral injection of Patent blue dye only was performed in 129 clinically T1-T2 and N0 breast cancers in 127 patients (Group A); it was later replaced by combined dye and radiocolloid-guided SNB preceded by lymphoscintigraphy in 74 breast cancer patients (Group B). All patients underwent completion axillary dissection. Group C comprises 50 patients, in whom axillary dissection was performed on the basis of the SNB.

Means of 1.4 and 1.3 SNs were identified in Groups A and B, respectively. The mean number of non-SNs for the whole series was 14.9 (range 5-42). The first 53 cases of lymphatic mapping (dye only) comprised the institutional learning period, during which the identification rate of at least 1 SN in 30 consecutive attempts reached 90%. The identification rate for the subsequent 76 Group A patients was 92%. The accuracy of SNB for overall axillary nodal status prediction and the false-negative rate for Group A patients (after exclusion of the learning-phase cases) were 93% and 10%,

respectively. All 74 Group B cases had at least 1 SN identified, and only 1 false-negative case occurred in this group, i.e. the accuracy and false-negative rate were 99% and 3%, respectively. Axillary dissection could be avoided in 25 patients of group C, was performed at the same time as the SNB in 15 and as a second operation in 10. Till now, no axillary recurrence was detected in group C patients, although the follow-up period is short for the moment.

The dye only and the radioguided SNB methods are complementary, their combination improves the performance, and can be the basis of performing axillary dissection on the basis of SNB results.

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POSTER

### Radioguided localization of non-palpable breast lesions and simultaneous sentinel lymph node mapping

A. Barros, J.R. Piato, A.C. Nisida, J.A. Pinotti, K. Pincerato, A. Vigário.  
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A new strategy of radioguided breast surgery combining ROLL and SLN mapping is presented. In 38 patients with mammographic non-palpable lesions (BI-RADS 4 and 5) it was injected at the lesion center 0.5 ml of a solution with dextran and 15 MBq of 99m Tc on the day before surgery. The patients were submitted to open surgical biopsy guided by probe, radiographic control of the specimen, frozen sections and SLN biopsy when necessary. The rates of lesion removal and simultaneous SLN mapping were 100% and 97.3%. In the first 8 malignant cases SLN and other axillary nodes were dissected, in the last 5, only SLN was dissected. In all of them intraoperative and definitive SLN analysis were negative, as well as the other dissected nodes. It is concluded that ROLL and SLN can be used simultaneously in non-palpable breast lesions allowing many advantages over the conventional procedures.

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POSTER

### Accuracy of sentinel node biopsy in predicting nodal status in patients with breast carcinoma

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**Background and Purpose:** Sentinel node biopsy (SNB) has been gaining popularity as an accurate axillary staging procedure. We retrospectively analyzed our data with the following purposes: 1) to assess the relation of axillary lymph nodes (ALN) and sentinel nodes (SN) metastases to the pathobiological characteristics of the primary tumor evaluated by postoperative histological examination, in order to develop a panel predictive for the SN status; 2) to evaluate the safety of avoiding ALN dissection (ALND) in patients with negative sentinel node biopsy (SNB).

**Patients and Methods:** We performed lymphatic mapping and SNB using the gamma detecting probe on 145 patients with T1-T2 breast cancer and clinically negative axilla. All patients underwent either quadrantectomy or mastectomy based on the size of the tumor and complete ALND. We assessed the relation of ALN metastases and SN metastases to the following pathobiological characteristics of the primary tumor: size, grading (G), hormone receptors (estrogen and progesterone) status, proliferative index (Mib-1), lymphovascular invasion (LVI) and c-erbB-2 expression.

**Results and Discussion:** SNB was positive in 49 (33.8%) of the 145 patients. Concordance between SNB and ALND was 96.6% (sensitivity: 90.7%; specificity 100%; vpp: 100%; vpn 94.8%). Five (9.3%) of positive ALND were SNB negative: all of these patients were T \* 20 mm or G \* 2. 19% of positive ALND was T < 20 mm: nobody in this subgroup was G1/Mib-1 < 13%, c-erbB-2 negative. Many authors have investigated the predictivity of the pathobiological characteristics of the primary tumor on the ALN and SN status. In our series, LVI and tumor size were significantly associated with ALN involvement (p=0.001 and 0.023 respectively). In the full logistic regression model the area under the ROC curve was 76.5%.

**Conclusions:** The ability of SNB to predict ALN status is very high. Primary tumor characteristics had no predictive value when singularly analysed, though LVI and tumor size were significantly associated with SN and ALN metastases. Our data confirm the validity of SNB to avoid axillary dissection, nevertheless patients with tumor size \* 20 mm (T2) and negative SNB should be submitted to ALND.

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POSTER

### SLN biopsy in cases of breast carcinomas submitted to neoadjuvant chemotherapy

A. Barros, J.R. Piato, A.C. Nisida, J.A. Pinotti, K. Pincerato, A. Vigário.  
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The objective of this study was to evaluate the capacity of SLN in predicting axillary nodal status in breast cancer patients treated by neoadjuvant chemotherapy. A total of 89 cases of infiltrating carcinoma (T1-2, No) were submitted to breast surgery and SLN biopsy followed by full axillary dissection. On the day before surgery it was injected 15 MBq of 99m Tc labelled to dextran in the peritumoral area. SLN was identified by lymphoscintigraphy and excised by probe guidance. In 47 cases (group 1) the patients received 3 AC cycles previously to surgery and in 42 (group 2) surgery was performed without neoadjuvant therapy. In group 1, in 29 cases SLN were negative and among them there were 4 cases of other nodes involvement, and in 18 cases SLN was positive. The accuracy of SLN biopsy was 91.4% in group 1 and 100% in group 2, and false negative rate were 13.7% and 0% respectively. It was concluded that neoadjuvant chemotherapy impairs the capacity of SLN in predicting axillary status.

Wednesday, 20 March 2002

16:30-18:00

PROFFERED PAPERS

## Locally advanced and metastatic disease

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ORAL

### Weekly docetaxel as neoadjuvant treatment in stage II and III breast cancer. Final results of a phase II, multicenter GEICAM study

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**Purpose:** This phase II study evaluated the efficacy and safety of weekly docetaxel as neoadjuvant chemotherapy in women with breast cancer. Furthermore, the pathological complete response (pCR) was determined and correlated with molecular markers such as Her2/neu, estrogen receptor (ER) and Ki-67 labeling index.

**Patients and Methods:** Eligible patients had measurable stage II or III untreated breast cancer. Docetaxel 40 mg/m<sup>2</sup> was given intravenously once a week, for 12 weeks (wks) with a 2 wks rest after the first 6 wks. Tumor biopsies were performed before treatment to determine molecular markers status. Her2, ER and Ki-67 were analysed by immunohistochemical assay.

**Results:** A total of 56 patients were evaluable for efficacy and safety. Median age was 53 years (28-73). Patients had a median tumor size of 4.6 cm (2-11). Initial stage was II (87%) and III (13%). Pre and postmenopausal was very similar (44% vs 50%, respectively). A total of 649 infusions were administered with a median of 12 per patient (3-18). Median relative dose intensity was 100% for docetaxel. The overall response rate was 68% (29% complete response and 39% partial response). Surgery was performed in 52 patients of whom 9 (17%) achieved a pCR. Non-hematological toxicity was more common than hematological toxicity, with alopecia and asthenia the most frequently reported adverse events (89% and 77% of patients, respectively). Hematological toxicity was infrequent. One patient presented with grade 3/4 anemia, and 2 patients grade 3/4 neutropenia. Regarding of the molecular marker status and pathological response to docetaxel, there did not appear to be a correlation between pCR and status of Her2, ER and Ki-67. Although not statistically significant, none of the patients with Her2/neu-positive tumors achieved a pCR.

**Conclusion:** This is one of the first reports of weekly docetaxel as neoadjuvant treatment of stage II and III breast cancer. This regimen appears very active in terms of pathological response with manageable toxicity. In addition, in this trial the Her2/neu status showed no correlation with the pathological response to docetaxel.