between June, 2001 and March, 2009. We judged it as SLNs, LNs which we could detect the uptake of 99mTc-Phytate colloid radioisotope (RI) or the staining with indigocarmine blue dye. Also, we decided it as para-SLNs (specific non-SLNs), LNs which were no uptake of RI and no staining with blue dye, but swelling or palpable around the SLN. We performed histological examination by frozen section and cytological one by stamp smear as intraoperative examination.

Results: The average age of all patients is 56 years old. Of 441 cases, SLN was able to be detected in 420 cases (94.8%). Nine cases (42.9%) had ALN metastases, of 21 cases whose SLNs were not detected and ALNs were additionally dissected. Of 420 cases that we were able to identify SLN, in 57 cases (13.6%) SLN metastases were diagnosed as positive at intraoperative examination and we performed ALND for those cases. Of 363 cases whose SLN metastases were diagnosed as negative at intraoperative examination, in 154 cases para-SLN was removed and, in seven (4.5%) of 154 cases, para-SLN metastases were diagnosed as positive at intraoperative examination. 15 cases were diagnosed as positive on SLN metastasis by the histopathological exam with permanent sections, and the false-negative rate was 4.8%.

[Conclusions] Mean of observation time is 44 months, no case is found with local recurrence by now. However, it is significant that 7 cases of metastasis-positive para-SLN deserved 37.5% of the false-negative cases. Also, we can not deny the possibility that reliability of SLNB may decrease when metastasis occurred in SLN, because SLN metastasis is present with 50% of the 22 case that we can not detect. Therefore, it is so important that we investigate para-SLN to avoid axillary LN recurrence as much as possible.

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A simple 'pulsing' technique of massage to improve detection rates of Blue Dye sentinel nodes in breast cancer

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Background: Detection rates vary from 70% to 96% after injection and Guiliano's technique of massage in the blue dye alone method of sentinel node in breast cancer. Poor detection rate with blue dye alone has been one of the major limiting factor in its usage over the dual technique. Injection sites for blue dye vary from intradermal, intra or peritumoral to subareolar injections. Massage is normally done, as described by Guiliano, by rotatory movements of the hand over the injection site. Passage of the dye through the lymphatics is by passive movement. Lymphatics start in the interstitium as avalvular plexuses, then form valved precollecting channels. Entry into the avalvular plexus at start of the lymphatic pathway depends on interstitial pressure. Subsequent flow through valved lymphatics is also passive. Rotatory massage may be limited in aiding forward flow. A simple pulsing technique of massage is described which significantly improves detection rates.

Methods: 2 ml of 2.5% Patent Blue dye is injected in the subareolar free space. Massage is done by the surgeon, prior to scrubbing, for at least 2 minutes by intermittent vertical pulsing movement of the flat of the fingers of one hand on the nipple areolar complex. The axilla is approached in the standard surgical way usually about 10 minutes from the time of injection.

Results: A total of 242 consecutive sentinel node procedures were performed between September 2007 and October 2009. Blue nodes were retrieved in all but 3 cases (239/242) giving a detection rate of 98.7%. Of the 3 cases that failed to show a blue node 1 was in a very large lady which made surgery technically difficult. One had previous lumpectomy and axillary sample and one other failed to show a blue node (it was thought not enough time was given between injection and surgery).

Conclusion: A new and simple technique is described that significantly improves detection rates in blue dye method of sentinel node retrieval. The technique of vertical pulsing massage may be increasing the interstitial pressure better than the horizontal and rotatory technique thus improving uptake of the dye through the avalvular plexus into the precollecting channels. It would also seem plausible that the intermittent pulsing movement helps the forward fluid movement of the dye through the valved lymphatics thus enhancing detection rates.

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Three-dimensional multidetector-row computed tomographic lymphography for sentinel lymph node biopsy in breast cancer

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Background: Three-dimensional multidetector-row computed tomographic lymphography (3D MDCT-LG) is useful for visualizing lymph flow and detecting a sentinel lymph node (SLN). In this study, we evaluated the usefulness of 3D MDCT-LG for SLN biopsy in patients with breast cancer.

Methods: From July 2007 to February 2008, forty patients with breast cancer (N0) underwent 3D MDCT-LG one minute after injection of iohexol under the periareolar skin on the day before surgery. The location of the SLN was marked on the skin using the laser light navigator system of the CT. During the operation, SLN biopsy was performed through a skin incision on the marked place after periareolar injection of patent blue, followed by resection of the primary tumor and backup axillary dissection. The SLN was tagged separately from other nodes. All removed nodes were pathologically examined.

Results: SLNs were clearly visualized by 3D MDCT-LG in 30 (75%) patients and faintly in 10 (25%). The patients with faintly visualized SLNs were significantly older than those with clearly visualized SLNs (72 ± 13 vs. 56 ± 11, $P < 0.01$). SLNs were identified in 37 of 40 patients (92.5%). The accuracy was 94.4% (35/37), and the false negative rate was 15.4% (2 of 13). Metastases were histologically confirmed in SLNs of 14 (35%) patients who did not have metastases in the axillay region preoperatively.

Conclusions: Preoperative 3D MDCT-LG was as useful for SLN biopsy as the radiocolloid method. Combination of preoperative 3D MDCT-LG and blue dye technique facilitates quick and accurate identification of SLNs.

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Feasibility of primary systemic therapy to save axillary lymph node dissection in patients with initial axillary lymph node metastasis

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Background: Primary systemic therapy (PST) downstages up to 40% of initial documented axillary lymph node (ALN) metastasis. The present surgical treatment strategy after PST may neglect the fact that patients with complete tumor response in metastatic axillary lymph node (ALN) could have the chance of being spared from axillary lymph node dissection (ALND). The aim of this study was To evaluate the feasibility and accuracy of sentinel lymph node biopsy (SLNB) after PST among the group of patients with documented ALN metastasis at presentation. And, we compared the difference of SLNB accuracy according to clinical tumor response after PST.

Material and Methods: We analyzed 66 patients with documented ALN metastasis who underwent SLNB and concomitant ALND after PST. Axillary ultrasound (USG) was used to evaluate the clinical response of initial documented ALN metastasis after PST. Intraoperative lymphatic mapping was performed using blue dye with or without radioisotope.

Results: After PST, pathologic complete response rate in patients with metastatic ALN was 31.8%. The overall success rate of SLNB after PST was 87.9%, and the mean number of identified sentinel lymph node was 2.8 (1−8). There was no significant difference in success rate of SLNB according to age, clinical tumor size, type of PST, and clinical tumor response. Six patients with negative sentinel nodes had positive non-sentinel nodes after the final pathologic examination (false-negative rate: 15.4%). According to clinical tumor response in axillary metastases after PST, false-negative rate was 0% in clinical complete response group and 19.4% in residual axillary metastases group.

Conclusion: Our findings suggest that SLNB is feasible in patients with initial documented ALN metastasis that had clinically complete response for metastatic ALN after PST. Further investigation in a prospective setting should be also designed to confirm our results.

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Optimization of the intraoperative sentinel node procedure in breast cancer with one-step nucleic acid amplification (OSNA) method

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Background: Recently, a new procedure has been developed for the evaluation of sentinel node in breast cancer. It is based in amplification of mRNA of 19 Cytokeratin by a loop mediated amplification reaction (RT-LAMP) otherwise known as one-step nucleic acid amplification (OSNA).

The amplification reaction time takes only 16min, but the transportation of the node from the operating room, the dissection of the node from the

surrounding fat and the homogenisation and conditioning of the sample can lengthen the timing of the whole procedure.

Our objective is to describe our experience in order to optimize the timing of the intraoperative study.

Material and Methods: A registry of the times of every step from the extraction in the operating room of 84 consecutives sentinel nodes to the emission of the diagnosis was done. We divided the time in three stages. First, time from the operating room to the Pathology Dept. Second from reception, macroscopic study and processing until amplification begins. Third, time from this moment to the diagnostic report.

Results: A learning curve was appreciated during the present study.

In the first stage, the mean of time spent was of the 48.5 min, 37.9 min in the second stage and 31 min. in the third stage.

The previous knowledge of the surgical program allows the possibility to calibrate and prepare the reactive having every thing ready for the reception of the sentinel node. Besides, a call from the operating room to Pathology Dept. allows thawing all the reactives in order to begin the pathologic work up immediately after sentinel node arrival.

Conclusions: A learning period and designing a precise circuit for the new sentinel node procedure certainly improves the total time of intraoperative diagnosis.

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Predictive factors for non-sentinel lymph node metastasis in breast cancer patients with sentinel lymph node metastasis

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Background: Axillary lymph node dissection (ALND) remains the standard of care for breast cancer patients with a positive sentinel lymph node (SLN). However, in more than half of patients with positive SLNs lymph node metastases are only located in SLN. The aim of this study was to identify factors predictive of non-SLN involvement after a positive SLN.

Materials and Methods: The medical records of 70 breast cancer patients who underwent SLN biopsy and ALND were selected from a prospectively collected database and were reviewed for multiple clinicopathologic factors. The statistical significance for comparing two groups was determined by Fisher's exact test.

Results: The mean number of SLNs was 3.3 ± 2.3. Of the 70 patients with a positive SLN, 14 (20%) had metastases in non-SLNs. Approximately 96% of patients (21 of 22 patients) with SLN micrometastasis had no non-SLN metastasis. Of the 48 patients with SLN macrometastasis, 35 (72.9%) had no metastasis in non-SLNs. Univariate analysis showed a significant association between non-SLN involvement and size of SLN metastasis ($p = 0.024$), and the number of positive SLNs ($p = 0.047$).

Conclusion: Detailed pathologic examination of the SLN metastasis may increase precision in the selection of patients for further ALND. However, more additional factors need to be identified before in selected cases ALND as a surgical staging procedure can be omitted.

Univariate analysis of clinicopathologic factors for patients with Non-SLN metastasis

	p
Tumour size	0.182
SLN metastasis size	0.024
No. of positive SLNs	0.047
No. of negative SLNs	0.076
Histological grade	0.058
ER	0.345
PgR	0.333

352 Poster

Sentinel lymph node detection using intradermal microbubbles and contrast-enhanced ultrasound in a swine model and patients with breast cancer

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Background: Sentinel lymph node (SLN) identification using intradermal microbbubles and contrast enhanced ultrasound (CEUS) has been recently reported in swine models and patients with breast cancer. The objective of the present study was to investigate the dynamics of intradermally administered microbubbles as they gain access to afferent tissue lymphatics in pigs and traverse through breast lymphatics in patients with breast cancer.

Materials and Methods: Nine anesthetized healthy pigs were used for the study and 5 female patients with primary breast cancer were recruited. Pigs recieved intradermal injections of microbubble contrast agent in several territories to access lymphatic drainage to regional lymph nodes (LN). Patients had periareolar intradermal injection of microbubble contrast agent. Ultrasound examination was performed in real time Cadence Pulse Sequencing (CPS) mode with a Sequoia scanner.

Results: SLN were identified rapidly (less than 1 minute) and consistently in pigs. In all 5 patients with breast cancer, microbubble contrast agent entered breast lymphatic channels and travelled to draining ipsilateral axillary SLN within a time period of 3 minutes. Intradermal microbubble injection and CEUS were found to have perfect concordance with the Evans blue dye method in locating swine SLN.

Conclusions: In patients with breast cancer, the ability to map lymphatic drainage and identify SLN in the diagnostic period would enable targeted biopsy and may facilitate pre-operative axillary staging in patients with early breast cancer.

Thursday, 25 March 2010 18:15–19:15

POSTER SESSION

Side effects and sequelae of breast cancer

353 Poster discussion

Safety of letrozole and tamoxifen monotherapy: updated BIG 1-98

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Background: BIG 1-98 is a double-blind randomized trial comparing 5yrs of treatment with either letrozole (Let), tamoxifen (Tam) or sequences of Let and Tam as adjuvant therapy for postmenopausal women with endocrine-responsive breast cancer. Initial results demonstrated superiority of Let over Tam in significantly prolonging disease-free survival (DFS). After release of these results 25% of patients (pts) assigned to Tam selectively crossed over to Let. As presented elsewhere, updated results (median follow up 76 mos.) after adjusting for selective crossover showed Let was significantly superior to Tam for DFS, overall survival, and time to recurrence. This report describes safety results for the pts randomized to receive Let or Tam monotherapy (4,922 of 8,010 pts enrolled).

Methods: The analysis population for safety included 4,895 pts, excluding 27 who received no trial treatment. Adverse events (AEs) were recorded during trial treatment or within 30 days of trial treatment completion. AEs, second (non-breast) malignancies, and deaths without prior cancer event occurring more than 30 days after selective crossover from Tam to Let were ignored. Prespecified AEs were collected and graded via check boxes every 6 months during treatment. Other AEs were coded according to MedDRA without knowledge of treatment assignment.

Results: In a competing risk analysis, the cumulative incidence of stopping treatment early due to an AE was 11.9% for Tam and 13.6% for Let (Gray's test $p = 0.08$). Pts on Tam experienced significantly more thromboembolic events, endometrial pathology*, hot flushes*, night sweats*, and vaginal bleeding. Pts on Let experienced significantly more bone fractures*, vaginal dryness, osteoporosis, carpal tunnel syndrome and arthralgia*. (*occurred in $\geqslant$10% of patients). Although the overall incidence of cardiac AEs did not differ significantly, higher grade cardiac events were more frequent on Let compared with Tam. The incidences of second (non-breast) malignancies (4.1% pts Let, 4.3% Tam) and deaths without prior cancer event (3.6% Let, 3.5% Tam) were similar.

Conclusions: As the AE profiles for Let and Tam differ, pts should be evaluated for baseline co-morbidities and monitored during treatment. Although a slightly higher percentage of pts stopped Let early due to AEs, Let continues to demonstrate superior disease control. Guidelines to monitor and manage bone health recently adopted may reduce the risk of bone fractures on Let.