Friday, 18 April 2008 12:30–14:30

POSTER SESSION

Local regional treatment/Surgery

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Fluorescence navigation system with indocyanine green for sentinel lymph nodes biopsy in breast cancer patients

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Background: Sentinel lymph nodes (SLN) biopsy is a useful method to assess axillary lymph node status in early breast cancer. Recently, a vital dye, radioactive tracer, or a combination of both is used to detect SLN. The dye-guide method is convenient and safe compared with the radioactive tracer-guided method, but lower identification is a problem. Indocyanine green (ICG) fluoresces by irradiating the excitation light when it unites with the serum protein. In the study, we present a novel method that allows the detection of SLN with high sensitivity using ICG fluorescence imaging.

Material and Methods: After the induction of general anesthesia, the combination dye of ICG and indigocarmine was injected intradermally in the areola for 0.5 ml. Fluorescence imaging device (Photodynamic Eye: Hamamatsu Photonics Co., Hamamatsu) was obtained using a charge coupled camera and light emitting diodes at 760 nm as the light source. Subcutaneous lymphatic channels draining from the areola to the axilla or other directions were visible by fluorescence imagings immediately. The SLN were then dissected by fluorescence navigation.

Results: This study enrolled 52 patients with clinically node-negative breast cancer. Their average age was 52.3 years. There were 32 cases with T1 lesions and 20 cases with T2 lesions. Subcutaneous lymphatic channels and SLN were successfully visualized in all patients. One lymphatic channel to the axilla was 71% (37/52), two channels were 25% (13/52), and three channels were 4% (2/52). The channels to other directions were not seen. The number of fluorescence SLN ranged from 1 to 6 (mean: 2.9), and blue dyed SLN ranged from 0 to 3 (mean: 0.9). In the latter, SLN were not identified in 19 patients (identification rate: 63%). Thirteen patients had lymph node metastases pathologically. All of them were recognized by fluorescence imagings, but, in three patients, lymph nodes with metastases were not identified by a vital dye. There were no intraoperative or postoperative complications associated with SLN identification.

Conclusions: This ICG fluorescence imaging technique is feasible and safe to detect SLN with less invasive and real-time observation. We hope that this method will provide with detection rate and negative predictive value in SLN navigation surgery.

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Predicting the individual clinical benefit of prophylactic bilateral mastectomy and oophorectomy in BRCA carriers with breast cancer

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Background: Breast cancer patients with a BRCA mutation have a markedly elevated risk for new cancers. Health care providers must communicate complex information about risk-reducing surgeries. We created models that provide individualized 5-year breast cancer survival and contralateral breast cancer predictions and the benefit of prophylactic mastectomy and oophorectomy.

Method: The study population was 491 women treated for stage I or II breast cancer between 1975 and 2000 and who had a known mutation or were from a family with a documented mutation (BRCA1, n = 327; BRCA2, n = 152; both BRCA1 and BRCA2, n = 12). The independent variables were age (less than 50 years old vs. 50 years old or older), tumor size (continuous variable), ER status (present vs. absent), and lymph node status (present vs. absent). Logistic regression was used to create the models. The output of one model was the probability of each outcome for bilateral mastectomy, and the output of the other model was the probability of each outcome for oophorectomy. Accuracy is assessed by the ROC.

Results: See the table. The 5-year breast and ovary cancer-specific survival model did not differ significantly from the 5-year breast cancer-specific survival model and is not reported here.

	Risk reduction mastectomy (RRM)	Risk reduction salpingo-oophorectomy (RRSO)
5-year breast cancer-specific survival	Model ROC = 0.707 RRM was not significant	Model ROC = 0.804 RRSO was significant
5-year contralateral breast cancer	Model ROC = 0.749 RRM was significant	Model ROC = 0.611 RRSO was not significant

Conclusions: In BRCA positive women with breast cancer, the model of risk reduction mastectomy for 5-year contralateral breast cancer and the model of risk reduction salpingo-oophorectomy for 5-year breast cancer-specific survival were highly accurate predictors of an individual woman's risk of contralateral breast cancer and disease-specific survival. These preliminary results await validation on an independent dataset. The individualized output of the predictive models will then be incorporated into a decision support tool for use in cancer risk counseling.

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The significance of the Van Nuys Prognostic Index in the management of ductal carcinoma in situ

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Background: Debate regarding the benefit of radiotherapy after local excision of ductal carcinoma in situ (DCIS) continues. The Van Nuys Prognostic Index (VNPI) is thought to be a useful aid in deciding which patients are at increased risk of local recurrence and may benefit from adjuvant radiotherapy (RT). Recently published interim data from the Sloane project has showed that the VNPI score did significantly affect the chances of getting planned radiotherapy in the UK, suggesting that British clinicians may already be using this scoring system to assist in decision making. This paper independently assesses the prognostic validity of the VNPI in a British population.

Materials and Methods: A retrospective review was conducted of all patients (n = 215) that underwent breast conserving surgery for DCIS at a single institution between 1997–2006. Kaplan Meier survival curves were calculated for the total sample and for a series of univariate analyses examining various prognostic factors including the VNPI. The log rank test was used to determine statistical significance in differ survival rates. All analyses were conducted using SPSS software, version 14.5.

Results: The observed and the actuarial 8 year disease free survival rates in this study are 91% and 83% respectively. The VNPI and the presence of comedo necrosis were found to be statistically significant prognostic indicators.

Conclusions: This study of 215 patients with DCIS who were treated with local excision and observation alone is one of the largest series in which recurrence is unaffected by radiation therapy, hormone manipulation or chemotherapy. It has therefore afforded us the opportunity to assess the prognostic impact of patient and tumour characteristics free of any potentially confounding treatment related influences. The results suggest that the VNPI can be used to identify subsets of patients who are at elevated risk of local recurrence and may potentially benefit from RT.

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Surgical aspect in NOAH Phase III trial (neoadjuvant trastuzumab in HER2-positive locally advanced breast cancer)

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Background: Patients (pts) with locally advanced breast cancer (LABC) are typically treated with primary chemotherapy, being not eligible for immediate surgery, mastectomy being the recommended approach. Here we present data from pts with HER2-positive LABC included in the randomized phase III NOAH trial.

Methods: 228 pts with HER2-positive LABC randomly received neoadjuvant chemotherapy [CT] (3 cycles of doxorubicin–paclitaxel [AT], A 60 mg/m^2, T 150 mg/m^2 q3w, 4 cycles of T [175 mg/m^2 q3w], and 3 cycles of cyclophosphamide/methotrexate/5 fluoracil [CMF]: C 600 mg/m^2, M 40 mg/m^2, F 600 mg/m^2 q4w on days 1 and 8) plus concomitant Herceptin®; H (8 mg/kg loading dose then 6 mg/kg q3w for 1 year) before surgery [115 pts] or the same chemotherapy only [113 pts]. In parallel 99 pts with HER2-negative LABC received the same CT. The primary end point is event-free survival (data maturing); secondary end points included overall response rate (ORR), pathological complete response (pCR) and overall survival. We report here updated ORR and the percentage of pts in whom breast conserving surgery (BCS) became feasible after primary neoadjuvant treatment.

Results: Improvement of pCR with H (43% vs 23%) in NOAH trial was already reported (ASCO 2007, abstr. 532). In the intent-to-treat population the updated ORR was 89% for the trastuzumab+CT group vs 76% for the CT alone group ($p = 0.012$). After 10 cycles of neoadjuvant therapy, 96 pts (83.4%) from H+AT/T/CMF group and 88 (77.8%) from CT-alone group underwent surgery. Adding H to AT/T/CMF improved rate of BCS (23% vs 12.5%, $p = 0.07$). Furthermore, in the subgroup of patients who achieved a clinical response (>50% tumour size reduction), this improvement was significant (24.7% vs 10.8%, $p = 0.02$).

Conclusion: Addition of H to neoadjuvant CT significantly increased ORR, led to downsizing of HER-positive LABC, thus allowing for more surgical options, and doubled the rate of BCS compared with CT alone.

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External validation of a piecewise effect model of axillary lymph node involvement in elderly breast cancer patients

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Background: Conflicting data exist on the correlation between the presence of axillary lymph node metastasis (LN+) and increasing age in breast cancer. In a large database of a single center of 2227 consecutively treated patients with early breast cancer, a piecewise effect of age on lymph node involvement was found with an increase in lymph node involvement after age 70 mainly in smaller tumors (St-Gallen 2007). The statistical model was now prospectively investigated in an external database.

Patients and Methods: The population-based Eindhoven Cancer Registry was used to validate the prediction model. It contains data from 11061 women with early breast cancer diagnose between 1-1-2000 and 1-1-2006, and for 3448 pts data on age, tumor size and lymph node status were available.

Results: The piecewise effect and tumor size dependence was confirmed. Lymph node involvement decreases up to age 70 (OR per decade increase in age = 0.764, 95% CI = 0.732−0.797) while for age $\geqslant$70, there is an increase with increasing age (OR 1.554, 95% CI = 1.371−1.761). There was a significant interaction with tumor size ($p = 0.0182$) where this increase in lymph node involvement after age 70 was only seen in smaller tumors ($\leqslant$20 mm).

Conclusion: Axillary lymph node involvement decreases with increasing age until the age of 70y, but then increases again. This increase after age 70 is only seen in the smaller tumors and suggests a different behavior of small breast cancers in elderly patients.

We hypothesize that on the one hand, breast tumors may metastasize less frequently to lymph nodes with increasing age due to the decreased biological aggressiveness in these tumors. On the other hand, if the tumors have the potential to metastasize to lymph nodes in elderly, this occurs more rapidly in smaller tumors and this may be related to decreased immune defense mechanisms in elderly patients.

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Elderly breast cancer patients treated by conservative surgery alone and adjuvant tamoxifen: 15 years results of a prospective study

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Background: In elderly patients with early breast cancer and clinically clear axilla, axillary surgery, sentinel node biopsy and post operative radiotherapy to the residual breast may not be necessary because of reduced life expectancy, effectiveness of hormone therapy in achieving long-term disease control and generally favourable biological behaviour of breast cancer in elderly patients.

Methods: We followed 354 prospectively recruited women aged 70 years or more with primary operable breast cancer and no palpable axillary nodes treated by conservative surgery and adjuvant tamoxifen, without axillary dissection or postoperative radiotherapy. Cases with resection margins in tumor tissue were excluded.

Endpoints were cumulative incidence of axillary disease, cumulative incidence of ipsilateral breast tumor recurrence (IBTR) and breast cancer mortality.

Results: Pathological stage at presentation showed pT1 size in 274 (77.4%) patients, pT2 ($\leqslant$3 cm) in 59 patients (16.7%) and pT4 b ($\leqslant$2.5 cm) accounted for 6% of cases. Infiltrating ductal carcinoma represented more than 65% of all histological types. ER and PgR receptor status was available for 331 patients; of these, 310 (94%) patients were ER +, 227 (69%) were PgR +, 224 (68%) were ER + and PgR + and 18 (5%) were ER − and PgR −.

After a median follow up of 15 years (interquartile range 14−17) crude cumulative incidences were: 4.2% (4.0% in pT1) for axillary disease, 8.3% (7.3% in pT1) for IBTR, and 17.0% for breast cancer mortality. Of the 268 patients who died during follow up, 222 (83%) died from causes unrelated to breast cancer.

Conclusions: Elderly patients with early breast cancer and no palpable axillary nodes may be safety treated by conservative surgery without axillary dissection and without postoperative radiotherapy, provided that surgical margins are in tumor free tissue and hormonal therapy is administered. Sentinel node biopsy is also unnecessary due to the low cumulative incidence of axillary disease and axillary surgery can be reserved for the small proportion of patients who later develop overt axillary disease.

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China multicenter study of sentinel node biopsy substituting axillary node dissection: CBCSG-01 trial

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Background: China multicenter study of sentinel lymph node biopsy (SLNB) substituting axillary lymph node dissection (ALND) in breast cancer – CBCSG-01 trial was conducted from Jan. 2002 to Jun. 2007, with 1,970 SLNB pts recruitment. The primary objectives were 5ys DFS and complications between SLNB and ALND. The second objectives included 5ys OS, SLN intraoperative diagnosis, micrometastasis detection and prognosis, and radiologic safety.

Materials and Methods: Combined methylene blue dye and 99mTc-sulfur colloid or 99mTc-IT-Rituximab were used as tracers for SLNB. Preoperative lymphscintigraphy was mandatory for all pts. Pts with negative SLN did not receive ALND.

Results: The median age was 46ys. The median number of SLN was 2. Tumor size was less than 5 cm, with mean size as 1.9 cm. With the increase of the size and advance of the histopathology of the primary tumor, the positive rates of the SLN increased significantly ($p = 0.000$, both). The surgical types were as follows: BCS+SNLB 51.4%, Mastectomy+SLNB 26.1%, BCS+ALND 8.9%, and Mastectomy +ALND 13.6%, respectively. Mainly due to the difference of primary tumor sizes, the rates of BCS, SLNB substituting ALND, and the positive rate of SLN were different among different centers. With a median fellow-up of 42 months in one early center – Shandong Cancer Hospital, two cases of axillary relapse (0.82%) were found in 244 SLNB cases ($p > 0.05$), while the complications of SLNB were significantly lower than that of ALND ($p < 0.001$).

Conclusions: 1) First in China to conduct prospective, multicenter study for SLNB substituting ALND for clinically early stage breast cancer, with 1970 cases enrolled; 2) Combined methylene blue dye and 99mTc were used as tracers for SLN, with the successful rate of 99.5%; 3) SLNB technique could avoid ALND for SLN negative pts (77.8% of clinically axillary negative cases in our study); 4) SLN positive rates increased significantly with the increase of the primary tumor size, which indicated that pts with small tumor should be selected first for SLNB substituting ALND in fresh hands; 5) The SLN positive rate was 3.5% in DCIS, which