

test. In the ROC curve analysis, the AUC was 0.823 (95% CI 0.720–0.926,  $p < 0.001$ ).

**Conclusions:** We developed and validated a web-based nomogram to predict post-operative invasive component in pre-operative DCIS in core biopsy. This tool will be helpful about decision to do a sentinel node biopsy in first operation of DCIS in core biopsy.

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Poster

#### Comparison of Clinicopathologic Features of Invasive Lobular Carcinoma of the Breast with or Without Associated Lobular Carcinoma In-situ

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**Background:** In breast cancer, invasive ductal carcinoma (IDC) with co-existing ductal carcinoma in-situ may be characterized by clinicopathologic and immunohistochemical features distinct from pure IDC, suggesting different biology and carcinogenesis. On the other hand, invasive lobular carcinoma (ILC) is believed to arise through linear histological progression, via lobular carcinoma in situ (LCIS), and ILC with concomitant LCIS (ILC-LCIS). However, comparison of pure ILC versus ILC-LCIS has not been reported.

**Material and Methods:** We analyzed a consecutive cohort of ILC patients undergoing upfront surgery in a tertiary referral center in Hong Kong between August 2001 and August 2011. Clinicopathologic features and immunohistochemical expression profiles of pure ILC were compared against those of the invasive component of ILC-LCIS, adjusting for invasive tumor size.

**Results:** A total of 144 patients were included in the analysis. All were female; median age was 50 (range 34–82). ILC-LCIS was associated with a smaller tumor size than pure ILC ( $p = 0.004$ ). After adjusting for invasive tumor size, there was no statistically significant difference between pure ILC and ILC-LCIS, in terms of tumor grade ( $p = 0.600$ ), lymphovascular infiltration ( $p = 0.831$ ), lymph node status ( $p = 0.332$ ), and expression profile of ER ( $p = 0.457$ ), PR ( $p = 0.290$ ), HER2 ( $p = 0.137$ ) and Ki67 ( $p = 0.831$ ).

**Conclusion:** Clinicopathologic features and immunohistochemical expression profiles were similar in size-adjusted pure ILC and ILC-LCIS. This supports the hypothesized linear model of carcinogenesis in ILC.

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Poster

#### Long-term Survival of Women with Carcinoma in Situ in Relation to HMG-CoA Reductase Expression

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**Introduction:** The rate-limiting enzyme in the mevalonate pathway, 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoAR) was recently identified in invasive breast cancer demonstrating a prognostic value, and, in tamoxifen treated patients, even a predictive value. Moreover, HMG-CoAR is the target for cholesterol lowering therapy with statins, and thus being a potential predictive marker for statin therapy in e.g. early breast cancer. Consequently, the expression and the prognostic value of HMG-CoAR should be evaluated in DCIS in parallel to former HMG-CoAR studies on invasive breast cancer.

**Aim:** The aim of this study was to examine the protein expression of HMG-CoAR in DCIS in relation to established pathological parameters and long-term survival data in a cohort of 458 DCIS patients.

**Methods:** The population-based cohort for this study, include women diagnosed with a primary DCIS between 1986 and 2004. Cytoplasmic staining of HMG-CoAR was assessed according to the staining intensity in the cytoplasm (negative, weak, moderate, strong) using tissue micro-arrays. The patients were followed until April 2008 and events were recorded as local /contralateral/general recurrence and death. For statistical analysis the Cox regression proportional hazards models were used to estimate the impact of HMG-CoAR expression on recurrence free survival (RFS) and overall survival (OS) in both uni- and multivariate analysis, adjusted for potential confounders.

**Preliminary Results:** In contradiction to invasive breast cancer, HMG-CoAR expression in DCIS was not statistically correlated to other tumor-specific characteristics (estrogen receptor, progesterone receptor, and HER2 status). Preliminary survival data with follow-up until April 2008 demonstrated 76 events of local recurrence (42 cases with in situ and 34 cases with invasive recurrence). Current data showed no statistical significant prognostic value with regard to HMG-CoAR. Updated results based on survival data with follow-up until October 2011 will be presented.

**Discussion:** Interestingly, this study on HMG-CoAR in DCIS could not demonstrate the prognostic value previously described in invasive breast cancer indicating differences in tumor biology. However, the number of events are currently few due to limited follow-up time, motivating the ongoing studies on recent survival data. If the preliminary results are confirmed, the potential differences in HMG-CoAR should be taken into considerations in future studies on statin therapy as preventional therapy.

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Poster

#### Postoperative Upstaging and Sentinel Lymph Node Metastasis in Patients with Ductal Carcinoma in Situ Diagnosed by Needle Biopsy

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**Background:** There is discordance between diagnosis of ductal carcinoma in situ (DCIS) by needle biopsy and postoperative pathological findings. The role of sentinel lymph node biopsy (SLNB) in patients with DCIS by needle biopsy is still controversial.

**Material and Methods:** We retrospectively analyzed 129 patients diagnosed with DCIS by needle biopsy who underwent surgery and SLNB in our institution from April 2007 to September 2011.

**Results:** Forty two (32.6%) of 129 patients were diagnosed with invasive cancer after operation. In univariate analysis, existence of ultrasonographic lesion, density on mammography (MMG), distortion on MMG, absence of microcalcification on MMG were correlated with postoperative upstaging. Nuclear grade, comedo necrosis and size of lesion on magnetic resonance imaging were not associated with the risk of upstaging. In multivariate analysis, ultrasonographic lesion was significant predictive factor of invasion (odds ratio (OR), 3.084;  $p = 0.016$ ). All patients received SLNB procedure but sentinel lymph node (SLN) was not detected in one case. Five of 128 (3.9%) patients had positive SLNs and all of them had invasive component in their primary lesions. In univariate analysis, density on MMG (OR, 12.966;  $p = 0.005$ ) and microcalcification on MMG (OR, 0.153;  $p = 0.024$ ) were significantly associated with the risk of SLN metastasis. Four (12.1%) of 33 patients with density on MMG and 3 (13.0%) of 23 patients without microcalcification had positive SLNs.

**Conclusion:** Postoperative upstaging in patients with initial diagnosis of DCIS was significantly correlated with the existence of ultrasonographic lesion. SLN metastasis was associated with density on MMG and absence of microcalcification on MMG. SLNB should be considered in patients with DCIS who have these predictive factors of invasive cancer.

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Poster

#### Open Controversies and Guidelines of the European Institute of Oncology (IEO, Milan) On the Management of Ductal Intraepithelial Neoplasia (DIN)

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**Background:** DIN is the new acronym (corresponding to ductal intraepithelial neoplasia) that replaces the traditional definition of ductal carcinoma in situ (DCIS) of the breast. Its incidence has increased in the last years, mainly due to the widespread use of mammography screening. Some aspect of DIN management are still controversial due to the heterogeneity of its clinical presentation and of its biological and pathological characteristics. The aim of this study is to describe not only the more widespread theoretical concepts on DIN but also the differences in the practical applications of the theory between different countries, different oncology specialists and different cancer centres.

**Material and Methods:** We analyzed papers related to the international multicentric-randomized trials and retrospective studies published in literature between 1993 and 2010; abstracts and reports from MEDLINE and other sources were identified. Our guidelines for surgery, radiotherapy (RT) and for systemic treatment are based on the analysis of 4.350 DIN

patients treated at the European Institute of Oncology in Milan between June 1994 and December 2009.

**Results:** The main goal of surgical treatment for women with DIN is breast conservative surgery (BCS); mastectomy is still indicated in large lesions, masses or microcalcification, in about 30% of cases. RT after BCS is indicated in selective cases, mainly depending on grading of the tumour. Medical treatment is proposed in estrogen receptors-positive patients. There are significant differences in the practical applications of the theory, in particular regarding the indications of sentinel lymph node biopsy, the definition and identification of low-risk DIN subgroups patient, which can avoid RT and tamoxifen and the identification of alternative drugs for adjuvant medical therapy.

**Conclusion:** New large trials are necessary to define the best management of DIN patients, because nowadays it still remains complex and controversial.

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Poster

### Clinical Differences Exist Between DCIS with Low and High Ki67 Expression

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**Background:** molecular characteristics as Ki67 expression could define different DCIS subtypes. The aim of this study was to establish clinical differences between DCIS expressing low Ki67 levels and DCIS expressing high Ki67 levels.

**Material and Methods:** we reviewed all DCIS treated in our institution between January 1993 and June 2011 (N = 256). Two groups were defined upon Ki67 expression: low expression group (expression in 14% of cells or less) and high expression group (expression in 15% of cells or more). Data on patient's age, menopause, breast cancer family history, breast symptoms, breast exploration, multicentric/multifocal disease and tumour size were collected. Microsoft Access and PASW statistics 18 were used to store and analyze data. Chi2, Fisher's exact test and Student T were applied when necessary.

**Results:** data on Ki67 expression were obtained in 79 patients. Patients in the high expression group were significantly younger (median±SD, 55.64±10.22 vs 60.68±11.43, p=0.05). More women in the high expression group were premenopausal (40% vs 26.7%), had a breast cancer family history (47.4% vs 24.1%) and presented a multifocal/multicentric disease (6.5% vs 2.1%), even though these differences were not significant. A similar percentage of patients in each group presented with breast symptoms (13% in the low expression group and 13.3% in the high expression group). A higher percentage of patients in the low expression group presented a positive clinical breast exploration (22.9% vs 12.9%) even though this difference was not significant. Tumour size tended to be bigger in the high expression group (median 27.70 vs 16.6 mm), but this difference was neither significant.

**Conclusions:** DCIS with a high Ki67 expression presents at a younger age than DCIS with low Ki67 expression. The study should include more patients for conclusive findings, but the group of high Ki67 expression showed a tendency to affect more frequently premenopausal patients and patients with a breast cancer family history. These high Ki67 expressing tumours also tended to present more frequently as a multifocal/multicentric disease and more extensive tumours.

Friday, 23 March 2012

12:45–14:00

### POSTER SESSION

### Radiotherapy

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Poster discussion

### Re-irradiation Plus Hyperthermia for Recurrent Breast Cancer in Previously Irradiated Area; Size Matters

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**Background:** Treatment options for patients with locoregional recurrent breast cancer in previously irradiated area are limited. Five hundred and

eighty-three patients were treated with re-irradiation and hyperthermia (re-RT/HT) in the AMC (n = 456) and the BVI (n = 127) from January 1982 till January 2006. Response, locoregional control and toxicity were analysed as well as prognostic factors.

**Materials and Methods:** All patients received extensive previous treatments, including surgery, chemotherapy and irradiation to a median dose of 50 Gy with or without boost. Median interval between initial treatment and re-RT-HT was 50 months (range 3–469).

The median age was 57 years at start of re-RT/HT. The estimated tumour size was >10 cm in 60% of patients. The maximum measurable tumor size was 50 cm. Distant metastases were present in 38% and 74% had experienced 1–14 recurrence episodes, prior to the re-RT-HT. Re-RT consisted typically of 8x4 Gy, twice a week (AMC) or 12x3 Gy, four times a week, (BVI). Superficial hyperthermia was added once/twice a week using 434MHz CFMA antennas. Aim temperature: 41–43°C for one hour. Twenty-two percent of patients received additional chemotherapy and 30% additional hormone therapy.

**Results:** Overall clinical response rate (50% cCR+ 32% cPR) was 82%. The infield 3-year local control (LC) rate was 20%. Tumor size, interval, previous recurrences, contralateral disease and distant metastases (DM) were important prognostic factors. For patients with isolated locoregional recurrences ≤ 5 cm the 3-year LC rate was 44%. (Table 1).

Median overall survival was 12.5 months. Acute ≥ grade 3 toxicity occurred in 26% of patients. The actuarial late ≥ grade 3 toxicity rate was 28% at 3 years.

Table 1

Tumor size	Isolated			With DM		
	n	cCR (%)	3-y LC (%)	n	cCR (%)	3-y LC (%)
≤ 5 cm	63	81	44	29	52	21
5–10 cm	88	60	24	53	36	20
>10 cm	204	51	15	141	30	10

\*Data unknown for 5 patients.

**Conclusion:** The combination of re-irradiation and hyperthermia results in high response rates despite extensive disease and resistance to previous treatments. Early referral is needed to achieve long term locoregional control. Currently a randomized phase 2 study of RT-HT versus RT-HT and CisDiamineDichloroPlatinum is performed to further improve results.

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Poster discussion

### Pre-operative CT Scan in Breast Conserving Therapy for Determination of the Boost Volume for Radiotherapy

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**Background:** There is a large interobserver variation of the boost volume delineation on the post-operative (post-op) radiotherapy planning CT scan. The aim of this study was to investigate whether a pre-operative (pre-op) contrast enhanced CT scan (CE-CT) can improve the accuracy of the boost volume delineation.

**Material and Methods:** Twenty patients with early breast cancer, planned for breast conserving surgery (BCS), underwent a pre-op CE-CT. After BCS a post-op radiotherapy CT scan was made in the same position.

A radiation oncologist and two physician assistants delineated the boost volume on the post-op CT scan (BVpost) without knowledge of the pre-op CE-CT. Minimally one month later the delineation was repeated (BVpre) after matching the pre-op CE-CT with the post-op CT on bony anatomy.

A radiologist delineated the tumour on the pre-op CE-CT, to assess tumour visibility.

Breast contour changes were analyzed.

All delineated boost volumes were measured, the average of BVpre and of BVpost was calculated.

The conformity index (CI = overlapping volume/encompassing volume) was calculated for both BVpre and BVpost, for each patient and for each observer pair (interobserver).

The center of mass distance (COMD) between BVpre and BVpost was calculated for each patient, and each observer pair.

**Results:** There was agreement on tumour visibility and location between all 4 observers in 19 of 20 patients on the pre-op CE-CT. These 19 patients were analyzed.

In 3 patients the projection of the tumour on the post-op CT scan was partly outside the body contour, due to contour change after surgery.

The mean BVpre (34.7 cc) and BVpost (37.6 cc) were not significantly different.

The interobserver CI showed a significant (p = 0.03) increase from 0.59 to 0.68 when the pre-op CE-CT was used. A significant (p = 0.01) decrease