

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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#### 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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#### 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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#### 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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#### 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