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Surgical resection of residual microcalcification after a diagnosis of pure flat epithelial atypia on core biopsy: a word of caution

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Background: The entity of pure flat epithelial remains a challenge due to controversy of the surgical management of residual microcalcifications after core needle biopsies. Our study aims to assess the morphological data observed in immediate surgical resection specimen of residual microcalcifications after a diagnosis of pure flat epithelial atypia on mammotome core biopsy.

Material and Method: Sixty-two mammotome core biopsy with a diagnosis of pure flat epithelial atypia (flat epithelial atypia without associated atypical ductal hyerplasia, in situ and/or invasive carcinoma) were identified. From these 62 cases, 20 presented residual microcalcifications and underwent an immediate surgical excision after mammotome.

Results: Of the 20 patients with excised microcalcifications with excised microcalcifications, 8 (40%) cases had residual pure flat epithelial atypia, 4 (20%) had atypical ductal hyperplasia, 4 (20%) had lobular in situ neoplasia, no lesion was retrieved in 4 (20%) case. None of the patients had either in situ ductal carcinoma and/or invasive carcinoma.

Conclusion: Surgical resection of residual microcalcifications after the diagnosis of pure flat epithelial atypia on core needle biopsy remains still a debate. We review the literature. The present study shows no case of n situ ductal and/or invasive carcinoma on immediate excision excision of residual microcalcifications after mammotome core biopsies.

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MRI of the breast in patients with DCIS to exclude presence of invasive disease

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Background: Ductal carcinoma in situ (DCIS) is a pre-invasive breast lesion without the ability to metastasize. DCIS can, however, be associated with presence of invasive cancer. Core biopsy has been reported to underestimate presence of invasion in up to 20% of patients with preoperatively diagnosed DCIS. The aim of the current study was to evaluate the efficacy of preoperative MRI to discriminate between patients with DCIS who are at high risk of invasive breast cancer and patients at low risk.

Methods: Patients preoperatively diagnosed with DCIS on core biopsy (absence of invasion) were prospectively included. All patients underwent contrast-enhanced MRI of both breasts prior to surgery. MRI was interpreted with respect to morphology, early and late kinetics of contrast uptake. In addition clinical, mammographic, and histological features from core biopsies were assessed. All patients underwent breast surgery (wide-local excision or ablation). Univariate and multivariate analyses were performed to identify features associated with presence of invasion in the resection specimens. Chi-square statistics and receiver-operating characteristics (ROC) analyses were employed.

Results: One-hundred-and-thirty-seven DCIS lesions in 134 patients were included. Mean age was 52.6 years (range 27−84 years). Eighty-one lesions (59.1%) showed enhancement at MRI with a type-1 curve (continuous increase) in 12 (8.8%), a type-2 curve (plateau) in 22 (16.0%) and a type-3 curve (washout) in 46 lesions (33.6%). Twenty-three lesions showed invasive cancer on final histology. The most predictive features to exclude presence of invasive disease at multivariate analysis were absence of enhancement or a type-1 curve at MRI (negative-predictive value 98.5%; area-under-the ROC-curve: 0.80, $p = 0.00002$).

Conclusions: Complementing clinical and conventional imaging parameters, contrast-uptake kinetics at MRI provide high negative-predictive value to exclude presence of invasion. The technique shows potential to facilitate selection of patients with DCIS in whom sentinel node procedures should not be considered.

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Lobular and luminal ductal invasive carcinoma of the breast − comparative molecular analysis

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Background: Invasive lobular carcinoma (ILC) of the breast is the second most frequent type of breast carcinomas. The E-cadherin inactivation is an early and characteristic molecular alteration of lobular carcinogenesis.

Material and Methods: In order to get insight the other molecular alterations of ILC, comparative genomic hybridization array and transcriptomic analyses (Affymetrix U133A+B) of series of 21 lobular carcinomas and 41 ER positive luminal invasive ductal carcinomas (IDC) were performed.

Results: ILC and IDC shared highly recurrent regions of gains of the 1q12-q44 region in more than 60% of the cases, of 16pter-p11.2 (45% and 62.7% of ILC and IDC respectively) and regions of losses on chromosomes 16q11.2-q24.2 (84.4% of ILC and 67.5% of IDC) and 17pter-p12 (50% of ILC and 49% of IDC). However, ILC genomic signature was characterised by significantly more frequent losses of the 13q21.33-q31.3 region (46.5%) and the 22q11.23-q12.1 region (50%) whereas IDC showed significantly more frequent losses of 11q23.1-q23.2 region, observed in 44% of IDC. Nine different regions of high level amplifications were found in 38% of ILC cases (8/21 cases). One region of amplification is observed in five ILC, localized on chromosome 11, (11q13.2 region) encompassing the *CCND1* and *FGF3* genes. Unsupervised hierarchical clustering of transcriptomic data showed that ILC and IDC clustered apart. Genes involved in cell adhesion, cell communication and trafficking, extra cellular matrix-interaction pathways or cell mobility contributed to this clustering. Some genes involved in chromatin maintenance were also differentially expressed between the two groups. Despite these differences, the overall outcome of ILC was identical to that of IDC.

Conclusion: This molecular study highlights that lobular and luminal ductal invasive carcinomas share common genomic alterations but that lobular carcinomas present some specific biological alterations and thus represent a distinct molecular entity. In addition, these molecular specificities should help with the identification of new therapeutic targets for ILC patients.

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Incidence of ductal carcinoma in situ: in the period before, during and after implementation of a population-based screening program

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Background: The Norwegian Breast Cancer Screening Program (NBCSP), a nationwide organised breast cancer screening program for women aged 50−69 years has gradually been implemented by county in the period 1995–2004. Studies in other countries have indicated associations between implementation of screening and increased incidence of pre-invasive breast cancer (Ductal Carcinoma *in situ*, DCIS). The aim is to study the effect of organised screening on trends in incidence of DCIS in Norway.

Material and Methods: Data were obtained from the incidence database of the Cancer Registry of Norway and the screening database of the NBCSP. All new pure primary cases of DCIS in the period 1993–2007 were retrieved as the basis of the study, $n = 3167$. Information about invitation to organised screening was given for the underlying female population, $n \approx 2.5$ mill, of which a quarter of the women have been invited to screening. The gradual implementation was utilized by restructuring the data according start-up of the NBCSP. To analyse the trends in incidence descriptive analysis and Poisson regression were used.

Results: The age-adjusted incidence of DCIS increased from 4/100 000 women-years before the implementation of organised screening (1993−4) to 11/100 000 women-years in the last period after implementation (2006−7). Correspondingly, the incidence increased from 11 to 31/100 000 women-years among women in the age-group of screening (50−69 years). After restructuring the data, a 70% increase in the incidence was seen in the pre-screening period ($p < 0.01$). After the prevalence peak at start-up of the NBCSP a further 30% increase was observed in the subsequent screening period ($p = 0.44$). The proportion of DCIS detected by screening has increased with time period, whereas 85% of the cases among women aged 50−69 years were detected by screening in the last period after implementation.