local excision and two (3%) mastectomy. Of those undergoing wide local excision seven (12%) subsequently underwent completion mastectomy and 10 (17%) re-excision. 14 (52%) of the cases in which histological size was >10 mm in excess of mammographic size required re-excision, compared with 2 (7%) of those showing <10 mm difference. Both of the two cases undergoing primary mastectomy had a histological size >10 mm in excess of mammographic size. Furthermore 14 (82%) of those requiring re-excision or completion mastectomy had a histological size >10 mm in excess of mammographic size. On review of slides, the discrepancy between histological and mammographic size appeared to be due to the presence of DCIS at the peripheries of the specimen that was not appreciated on radiological assessment because of the absence of microcalcification.

Conclusions: Our study demonstrates that there are discrepancies between histological and mammographic sizes and that such discrepancies result in an increased requirement for re-excision. It would appear that these discrepancies result because not all DCIS within a lesion is associated with microcalcification. We believe, therefore that, despite the extra workload, wide sampling and tumour mapping may be superior to specimen radiology alone.

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Contribution of cytological CSF analysis to the management of patients with breast cancer; a retrospective analysis over two decades

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Background: Metastatic spread of breast cancer to the central nervous system (CNS) is relatively frequent. Unequivocal diagnosis of such spread may be difficult as the neurological and radiological presentation are very diverse. Since long, cytological examination of the cerebrospinal fluid (CSF) is considered as a valuable, additional tool to prove the diagnosis of CNS metastasis of breast cancer. However, the exact value of CSF cytological examination for patient management is not clear.

Aim: To assess the contribution of cytological CSF analysis to the management of breast cancer patients.

Materials and Methods: In a single pathology department serving two breast cancer centre hospitals we retrieved information of all patients (n = 81) with a histological diagnosis of breast cancer that had at least one lumbar puncture in the period of Oct. 1989 to Oct. 2009 to allow for cytological CSF examination. Relevant information was retrieved from the clinical (esp. type and stage of breast cancer, neurological signs and symptoms) and radiological records. For cytological CSF analysis, a cytospin procedure was performed, the slides were Papanicolaou stained. The cytological diagnosis on CSF was classified in the categories proposed by the 1996 NCI-sponsored conference approach: malignant, suspicious for malignancy, atypical, benign and unsatisfactory.

Results: In 20 years 145 CSF examinations were performed in 81 breast cancer patients with a very diverse clinical and radiological context. Relatively frequent reasons to perform CSF examination were headache (n = 23), and spine or radicular pain (n = 12), in somewhat less than half of these patients malignant cells were detected in the CSF. A substantial number of patients without abnormalities on MRI (n = 20) and CT scans (n = 22) did have malignant cells in their CSF specimens (4 and 6, resp.). Repeated examination of CSF was performed in 37 patients (2−13 times) resulted in a change in cytological diagnosis from suspicious to malignant in only one patient.

Conclusion: This study underscores that cytological examination of the CSF is a very valuable tool for unequivocal diagnosis of metastatic spread to the CNS in breast cancer patients. Even in a substantial number of breast cancer patients with neurological symptoms but without radiological abnormalities on MRI and/or CT scans malignant cells are found in the CSF. In this study, the additional value of repeated cytological examination of CSF was very limited.

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Ki67 proliferation as a biomarker in neo-adjuvant breast cancer studies − core biopsy versus surgical sample

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Background: Proliferation is a key feature of tumor progression and is widely estimated by the assessment of the antigen Ki67 immunohistochemically. Ki67 is not only used as a static marker of proliferation, but also used as a marker of treatment efficacy. In neo-adjuvant breast cancer studies pre-treatment Ki67-index is assessed on material from either fine needle or core biopsies and compared with post-treatment Ki67-index in surgical samples. However, verification of the validity of Ki67 use to evaluate a treatment has not been previously studied. The aim of this study was to identify a potential baseline difference in Ki67-index between core biopsies and surgical samples in an untreated cohort.

Material and Methods: Tumor tissue from core biopsies and surgical samples from a retrospective consecutive cohort of 50 women operated for breast cancer was collected. The core biopsies and the corresponding operation samples were evaluated for proliferation through immunohistostaining of Ki67 using the MIB-1 antibody. Ki67 was examined on 2x, 10x and 40x magnification to identify hotspots, areas with increased number of Ki67 positive tumor cells. Using 40x magnification over the hotspot, 10 cancer cells at a time were counted covering the entire field of magnification or until 1000 cancer cells were evaluated. Each core biopsy and operation sample was evaluated twice with the counter blinded to the relationship between samples.

Results: Since no treatment was given during the intervening time between biopsy and operation, no significant difference in proliferation values was expected. However, preliminary results show that the proliferation in the biopsy samples was slightly (2%), but significantly (p = 0.04), higher than proliferation in the operation samples. In dichotomized analyses using the clinically used cut-off at 20% positive cells no significant difference between biopsy and operation sample was found. Statistical analyses further indicated that the number of cells needed to count in order to estimate proliferation index was 200 cells.

Conclusion: This study demonstrates a baseline decrease in proliferation index between core biopsy and operation samples, which needs to be taken into account when evaluating treatment efficacy in neo-adjuvant studies.

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Morphological and immunophenotypic analysis of triple negative breast carcinomas

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Background: Triple-negative breast cancer (estrogen receptor-negative, progesterone receptor-negative, and HER2-negative) is an aggressive disease without tumour-specific treatment options. Frequently they are associated with a basal phenotype. In the present study, we have analyzed the expression of basal markers and morphological characteristics in the triple negative breast carcinomas.

Method: A total of 117 consecutive cases of invasive ductal breast carcinomas diagnosed in our institution were screened for the triple-negative phenotype, and were subsequently evaluated for cytokeratins (CK): 5/6 and 17, p63, and c-kit immunoexpression. In addition, haematoxylin and eosin-stained sections of these tumours were studied for several morphological parameters such as appearance of tumour margin, the presence of lymphoid stromal infiltrate, comedo-type necrosis, and prominent central necrosis/fibrosis. The findings were correlated with patient and tumour characteristics.

Results: Triple negative breast carcinoma phenotype was found in 13.68% (16/117) in our series. Expression of CK5/6 showed 26 tumours (22.22%) and 35 (29.91%) were CK17-positive. Thirteen (11%) cases expressed c-kit, and sixteen (15%) showed p63 positive expression. A total of 11 (69%) triple negative tumours showed a CK5/6-positive expression, and 14 (87%) triple negative tumours expressed CK17 (p = 0.000). The triple negative cancers were different from the non-triple-negative carcinomas by having a high histological grade (75% versus 15%, p = 0.000), tumour size larger than 2 cm (49% versus 33% p = 0.06), and by pushing border (62% versus 10%, p = 0.000). No differences were seen for the presence of lymphoid stoma infiltrate, comedo-type necrosis, and prominent central necrosis/fibrosis. Also, c-kit expression was significantly higher in triple negative group than in non-triple negative group (p = 0.003), but no significant differences were found between triple negative and non-triple negative cancer group in relation to p63 expression.

Conclusions: Triple negative breast cancers differ from non-triple negative breast cancers in several aspects, and have a higher malignant phenotype. The majority, but not all, of the triple-negative breast carcinomas exhibit a basal-like phenotype. Thus, triple-negative should not be used as a surrogate marker for basal-like cancers. C-kit expression is more often present in the triple-negative tumour group than in non-triple negative cases. This data suggests that c-kit expression might be important as a potential target for molecular therapy in triple-negative breast cancer.