imaging modalities. They noted tumour size and localization as well as suspicion of multifocal or multicentric disease.
The information on the therapeutic strategy was retrieved from the patients' files. The size and extent of the tumour on MRI was used to plan the definite surgical treatment.
Results: A change in therapeutic strategy was obtained in 16 (46%) of the 35 patients. In 4 patients MR imaging showed a lager tumour size than was measured on clinical examination, mammograpy and ultrasound. In 8 patients a change in therapeutic management was made because of a multifocal tumour, which was suggested at MR imaging. Two patients had a change in surgical strategy because the tumour was diffusely spread towards the skin. One patient was diagnosed with a contralateral tumour and in one patient the MR imaging showed suspect lymph nodes in the axilla an aso xillary dissection was indicated.
Conclusion: In this series the initial surgical therapy was changed in 16 out of 35 patients with invasive lobular carcinoma because of additional findings on MRI. Therefore MRI should be a standard preoperative procedure in every patient with a lobular carcinoma.

2056 POSTER

A cross-study verification of breast cancer gene signature in peripheral blood

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Background: It has previously been reported a potential use of gene expression profiling in peripheral blood cells for early detection of breast cancer [1]. This potential was identified by means of internal double cross-validation within a dataset (DiaGenic set). Although cross-validation is a statistical sound method for model/predictor validation, a verification of the predictive ability on a set of independent samples is highly valuable.
Material and Methods: In the two studies reported here, high-density oligo-nucleotide arrays from Applied Biosystems have been used to track the changes in genetic activity in peripheral blood cells. As an independent sample set we used data that were created as part of a project aiming at increasing the knowledge about the biology underlying mammographic density and increased risk of breast cancer development (MDG set). Blood samples and biopsies (normal or tumor) were collected from patients with breast cancer and from women without breast cancer. Expression profiling of the blood samples were analysed in parallel with the DiaGenic set, using identical lab protocols, but in separate batches. Both data sets were pre-processed and batch adjusted in the same mannerA novel method called L-PLS-regression (Saebo et al. [2]) was used for prediction. This method utilizes background knowledge on the variables in the process of predictor construction in an attempt to reduce the influence from false positive genes and random noise. The predictor was trained on a subset of genes from the DiaGenic dataset under the influence of information on inter-gene dependencies extracted from the KEGG-data base [3].
Results: We will present results from the prediction of breast cancer status for the MDG patients that verify the internal cross-validation results for the DiaGenic data with respect to classification accuracy. We also show that an increase in accuracy may be achieved by exploiting background information in the process of predictor construction.
Conclusion: A gene expression profile for breast cancer in peripheral blood seems to give fairly good prediction of cancer status for independent samples run on the same microarray platform, despite the presence of both batch effects and effects of blood sampling location.

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Current national pathology guidelines for the examination of sentinel lymph nodes in breast cancer are insufficient for the detection of micrometastases

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Background: The extensive pathologic evaluation of the sentinel lymph node (SLN) in breast cancer patients resulted in a more frequent observation of micrometastases (MM). If these MMs are of prognostic relevance the sensitivity of the pathology examination should be sufficient. We calculated the probability of detecting MMs when examining the SLN according to the current Dutch pathology guidelines and tested alternative examination protocols.
Patients and Methods: We assessed the size of an axillary SLN in 20 patients with cT1−2N0 breast cancer and designed a mathematical model to calculate the probability of detecting MMs ($\geqslant$0.2 mm and $\leqslant$2 mm) in a SLN. For evaluating SLNs the Dutch pathology guidelines advocate to bisect a SLN and to take at least three cuts from both halves with 250 μm distance between two cuts. We used the mathematical model to test alternative examination strategies to optimize the chances of detection.
Results: When examining the SLN according to the Dutch pathology guidelines, the chances of detecting a MM with a size of 0.2 mm never exceeded 50 percent: the probability was 0.39 in the smallest SLN, 0.15 in the largest, and 0.24 in a SLN of median volume. The probability to detect a 2 mm MM was 0.99, 0.50 and 0.75 respectively.
To reach a sensitivity of 95% (of detecting a 0.2 mm MM) the interval between the cuts had to be 200 um and 11 cuts from both halves were required for the smallest SLN, 31 cuts for the largest SLN, and 19 cuts for the median-sized SLN.
Conclusion: The current guideline-based pathology practice to evaluate the SLNs is not sufficient for the detection of small lymph node metastases. Since lymphogenic MMs may be of prognostic significance adjusting the number of, and the interval between the cuts is advocated.

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Factors influencing survival of 107 HER2 positive breast cancer patients treated with trastuzumab based neoadjuvant chemotherapy

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Background: c-erb2 gene plays a crucial role in mammary cancerogenesis. Trastuzumab (T) based chemotherapy has been a revolutionary step in the HER2 positive breast cancer treatment.
Aims: to determine the factors correlating with disease free and overall survival in HER2 positive breast cancer treated with T based neoadjuvant chemotherapy.
Material and Methods: Data from two phase II were used: The TAX-HER trial which studied the use of 6 courses of 3 weekly docetaxel with weekly T (B Coudert, Ann Oncol 2006) and the GETNA1 trial which studied the use of 6 courses of 3 weekly docetaxel and carboplatine along with weekly T (B Coudert, JCO in press). For the GETNA1 trial, adjuvant T was used in case of responding tumor. Survival curves were estimated using Kaplan-Meier methods.
Results: 41 patients were enrolled in the TAXHER study. Tumor characteristics were as follows: 29 T2 (71%), 9 T3 (22%), 3 T4 (7%); 20 N0 (49%), 17 N1 (41%), 4 N2 (10%); 1 SBRI (2%), 22 SBRII (54%), 18 SBRIII (44%); 22 RH+ (54%), 19 RH− (46%). Surgery was conservative in 31 patients (76%). Pathological complete response (pCr) (Chevallier grade 1/2) was diagnosed in 17 patients (41%). With a median follow up of 50 months were diagnosed: 4 local recurrences with a median local disease free survival of 48 months [15−65], 10 metastatic recurrences with a median metastatic disease free survival of 48 months [12−65] and 3 deaths. 66 patients were enrolled in the GETNA1 study. Tumor characteristics were as follows: 46 T2 (70%), 17 T3 (26%), 2 T4 (3%), 1 unknown (1%); 29 N0 (44%), 36 N1 (55%), 1 N2 (1%); 1 SBRI (1%), 27 SBRII (41%), 33 SBRIII (50%), 5 unknown (8%); 33 RH+ (50%), 26 RH− (39%), 7 unknown (11%). Surgery was conservative in 42 patients (64%). pCr was diagnosed in 25 patients (38%). With a median follow up of 25 months were diagnosed: 5 local recurrences with a median local disease free survival of 25 months [11−43], 8 metastatic recurrences with a median metastatic disease free survival of 23 months [13−43] and 1 death.
Conclusions: Despite high pCr rates, obtained with trastuzumab based chemotherapy, HER2 positive breast cancer prognosis remains to be monitored. A multivariate analysis of the factors (tumor characteristics, type of chemotherapy, type of surgery, pCr, adjuvant trastuzumab) correlating with disease free survival and global survival in HER2 positive breast cancer treated with trastuzumab based neoadjuvant chemotherapy will be presented at the congress.