compared: tantalum > titanium ($p < 0.0001$), medium > small ($p < 0.0001$), and lower outer > other quadrants ($p = 0.004$). For floor mounted kV imaging, 98.4% MTa, 91.1% STa, 53.1% MTi, and 10.4% STi clips were clearly visible. For isocentric kV imaging, 99.0% MTa, 93.8% STa, 88.9% MTi, and 61.8% STi clips were clearly visible. For isocentric MV imaging, 94.8% MTa, 36.1% STa, 0% MTi, and 0% STi clips were clearly visible. The mean volume (cm^3) of artifact generated by MTa, STa, MTi, and STi clips was 0.81, 0.23, 0.07, and 0.01, respectively.
Conclusions: MTa clips were visualised best, but their CT artifact was unacceptable. STi clips were poorly visualised. Both MTi and STa clips proved suitable as fiducial markers for isocentric kV imaging, although MTi clips generate less CT artifact. STa clips were best visualised for floor mounted kV imaging.

2052 POSTER

Incidence of chemotherapy induced amenorrhea and the role of hormone therapy on ovarian function in hormone sensitive breast cancer

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Background: The incidence of chemotherapy-induced amenorrhea (CIA) and the importance of ovarian function (OF) in hormone sensitive breast cancer is not well defined. The aim of this study is to define the risk factors of permanent amenorrhea after chemotherapy in premenopausal patients, and the impact hormonal therapy has in OF.
Material and Methods: 323 premenopausal patients from our center, diagnosed with hormone sensitive (ER and/or PR positive) invasive breast carcinoma between January 1998 and June 2005 were selected. All received adjuvant or neoadjuvant anthracycline based chemotherapy, with or without taxanes, or high dose chemotherapy followed by autologous bone marrow transplantation (ABMT). The kind of hormone treatment received was also taken into consideration. The data was obtained from the medical records. The two main questions were the incidence of CIA among our patients according to the patient's age and chemotherapy schedule, and the restart of the OF during hormonal treatment.
Results: 255 pts with CIA, and 68 with no amenorrhea, were analyzed. The age distribution among patients with CIA was as follows: 45 yrs or older: 140 patients (95.2%), 40−45 yrs: 66 patients (71.74%), 35−40 yrs, 41 patients (61.1%), 35 yrs or younger: 8 patients (36.3%), $p < 0.0001$. A significant difference in CIA was found between the two groups ($p < 0.034$). 160 out of 212 patients in the anthracycline based chemotherapy group was found to have CIA (75.4%), while this was the case in 77 of 93 patients in the anthracycline and taxane group (82.8%) There was 100% amenorrhea in the group of 17 patients that received high dose chemotherapy followed by ABMT.
Of 148 patients with CIA and tamoxifen, 10 recovered OF: 7 were still on tamoxifen (4.7%), 3 patients had discontinued treatment (2%). Of 107 on aromatase inhibitors, 7 recovered OF (6.5%)
Conclusions: There is a direct correlation between the patients' age and chemotherapy schedule combining anthracycline and taxanes, and chemotherapy-induced amenorrhea. Aromatase inhibitors treatment was associated with a higher recovery rate of ovarian function.

2053 POSTER

Breast ductal lavage biomarkers in relation to estrogen response and risk factors

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Background: The importance of estrogen in breast cancer risk is amply confirmed by clinical data on the effectiveness of selective estrogen receptor modulators and aromatase inhibitors, yet measurements of plasma estrogen concentrations have not provided the expected degree of association with breast cancer incidence. This disparity may be explained by the poor correlation between plasma and breast fluid concentrations of estrogens and products of estrogen action. The present study provides an estimate of the association between a number of factors measured in ductal lavage fluid and risk as assessed by the Gail model.
Methods: Women at high risk for breast cancer were recruited (Gail score for 40 premenopausal women: 1.6−6.9, median 2.5; for 27 postmenopausal: 1.6−6.9, median 3.0). Ductal lavage was performed prior to treatment with tamoxifen. The cells were removed and the fluid was reduced to a volume of 1.0 ml for immunoassays of estradiol, estrone sulfate, androstenedione, DHEA, cathepsin D, and EGF. Significant factors from backward stepwise multiple regression for each group were determined after normalization by log transformation
Results: In premenopausal women with Gail score as the dependent variable, the model R2 was 0.207; estrone sulfate had a standard coefficient of 0.506 ($p = 0.003$) and EGF had a standard coefficient of −0.464 ($p = 0.008$). Other factors did not reach significance. In postmenopausal women with Gail scrore as the dependent variable, the model R2 was 0.356. EGF had a standard coefficient of 0.753 ($p = 0.003$) and DHEA had a standard coefficient of −0.524 ($p = 0.048$). Other factors did not reach significance. Cathepsin D was related to estrone sulfate in post- but not premenopausal patients. R2 was 0.243, and the standard coefficient was 0.493 ($p = 0.002$).
Conclusions: Gail scores in women at high risk for beast cancer are highly significantly related to components of breast fluid but the associations were quite different in pre- and postmenopausal women. An estrogen was an important predictor of risk in premenopausal women and EGF was the most important predictor of risk on postmenopausal women. The estrogen response protein, cathepsin D, was not related to estrogen in the same manner as risk.

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Acute effects on cardiac function after breast radiotherapy – a strain rate imaging study

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Background: Radiotherapy for breast cancer is associated with long-term cardiac dysfunction. Doppler Myocardial Imaging (DMI) has been shown to be a sensitive echocardiographic tool for quantifying subtle changes in cardiac function. This study investigates the occurrence of early radiation-induced changes in regional cardiac function by DMI.
Materials and Methods: In a pilot study, 15 women (age 54±14.4 years) with left-sided breast cancer were examined. All patients received radiotherapy to the breast or chest wall by respectively tangential photon beams or direct electron fields. In 8 patients, the internal mammary and medial supraclavicular (IM-MS) lymph nodes were treated by direct anterior mixed photon and electron beams. Dose prescription was 50 Gy in 25 fractions. In all patients, part of the cardiac apex was irradiated. Patients with an intact breast received an additional boost to the tumour bed of 16 Gy. Epirubicin containing chemotherapy was given to 9 patients prior to radiotherapy. Standard echocardiography and DMI data were obtained before and after radiotherapy. Peak systolic longitudinal velocity (VEL) and strain rate (SR) as well as systolic strain (S) were measured in all patients for the 18 mid, basal and apical left ventricular (LV) segments.
Results: Conventional and DMI data could be obtained in all patients before and after radiotherapy. LV dimensions, ejection fraction and other conventional parameters of systolic and diastolic function did not change after radiotherapy. Segmental VEL was also not different. In contrast, a significant reduction in S (21.5±7.3 to 17.8±7.6, $p = 0.001$) and SR (1.41±0.52 to 1.17±0.41, $p = 0.001$) was found after treatment only at the level of apical segments, but not in the basal or mid segments (−21.1±6.1 to −20.0±6.5 and −1.50±0.40 to −1.40±0.34, resp., both n.s.).
Conclusions: In contrast to conventional echocardiography, myocardial deformation parameters allowed the detection of regional decrease in myocardial function early after radiotherapy for left-sided breast cancer. Further follow up is needed to assess the relation between these early changes and long term dysfunction.

2055 POSTER

MR Imaging in the preoperative assessment of patients with lobular carcinoma of the breast

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Background: Infiltrating lobular carcinoma is the second most common breast malignancy and represents 7−15% of the invasive breast cancers. The diagnosis is however not without difficulties.
Lobular carcinoma shows a diffuse growth pattern of cellular infiltration, including linear file arrangement and a lack of desmoplastic reaction, necrosis or calcification. These typical histological characteristics may account for the existing imaging difficulties. Tumou rextent can be underestimated on mammography and ultrasound or multifocal disease can be missed.
In this study we retrospectively compared findings on preoperative MR imaging with mammography and US in 35 patients with lobular carcinoma and evaluated the effect on the surgical therapy.
Methods: 35 patients who were diagnosed with a lobular carcinoma between december 2003 and december 2006 and underwent pre-operative MR imaging were included. Two radiologists retrospectively reviewed all

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.

2057 POSTER

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.