Soroka), and 33 patients with liver, lung and lymph node metastases (doxorubicin or docetaxel; Nottingham). The population/drug-calibrated OVP was simulated, inputting each patient's initial data to predict individual disease course and hematopoietic toxicity under the given regimen. OVP prediction accuracy was calculated, blinding being ensured between data collection and simulations.
Results: average OVP prediction accuracy of the actual response in individual patients was 85%±9% and 70±5% in the Soroka and the Nottingham arms, respectively. Toxicity predictions were ranging from excellent to poor, as evaluated by success in recovery of neutrophil counts and day of nadir. In general, we could prove a good retrieval of day and counts of nadir as well as neutrophil peak levels in about 50% of patients whose counts were recorded frequently enough. Full statistical analysis is yet to be performed.
Conclusions: OVP showed a good accuracy in predicting response and toxicity of primary and metastatic breast cancer to AC-Taxol, doxorubicin and docetaxel chemotherapy. However, the poor efficacy prediction for some patients suggests need to evaluate new response biomarkers, as well as patients' pharmacokinetics variations.

O-104 Gene expression profiling of axillary node negative tumour tissues using microarrays to inform prognosis in breast cancer

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Traditional histopathological prognostic methods fail to accurately predict outcomes in early stage breast cancer. Several studies have used gene expression profiling to more accurately predict outcomes in breast cancer. The aim of this study was to analyse gene expression in breast tumours using microarrays and validate these results using quantitative real-time PCR (RQ-PCR).
Tissue from ten axillary-node-negative breast cancer patients with recurrence within five years were selected and matched for age, stage and treatment with 10 patients with no recurrence on long-term follow-up. Whole genome profiling was performed using the Applied Biosystems 1700 whole genome microarray. Seven genes, previously associated with outcome, were selected for further interrogation using quantitative real time PCR (RQ-PCR) in the same group of patients in order to validate the results of the microarray. RQ-PCR was performed using TaqMan chemistries and the ABI Prism 7000. Quantile-normalised intensities were used to calculate fold-changes in gene expression between prognostic groups. Associations between microarray fold-change and gene relative quantity following RQ-PCR analysis were analysed in multiple targets using Pearsons correlation coefficient (SPSS v.14).
Comparison of microarray and RQ-PCR confirmed associations between fold-changes for the different groups. Of the seven genes, GATA3 was over-expressed in good prognosis patients relative to poor prognosis ($p < 0.001$). In poor-prognosis patients GATA3 was over-expressed in ER-positive relative to ER-negative patients ($p < 0.01$).
Using this validated microarray data we have identified GATA3, which is associated with prognosis in breast cancer, further supporting a role for this transcription factor in breast cancer and hormone-regulation of this disease.

O-105 erbB Signalling in breast cancer

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Much interest has focused recently on the Epidermal Growth Factor Receptor (erbB) family, on the prognostic and predictive power of its members, their role in carcinogenesis and erbB directed therapies.
Early work has demonstrated that erbB plays a role in defining molecular subtypes. However, these data are restricted to only the erbB receptors (EGFR, HER-2, HER-3 and HER-4). No data exists on the entire family of receptors and ligands and clustering patterns which may exist in vivo.
Method: Using immunohistochemistry, we studied the combined protein expression profiles of 800 cases of primary operable breast cancers using a large panel of well characterized biomarkers for the erbB family. For each panel, the Pharm Dx® and the HercepTest antibodies was best linked to survival for EGFR and HER-2 respectively.
On the basis of these expression profiles tumours were stratified using hierarchical clustering algorithms into 5 groups. This tool reordered tumour samples into clusters with distinct patterns of protein expression. The clusters are displayed in a dendrogram in which tumours with the greatest similarity cluster together. Further analysis was performed using multiple layer perceptron (MLP)-Artificial Neural Network (ANN).
Results: Clustering showed broad similarity with previous studies based on cDNA and protein microarray. However, for the first time subcellular clustering of ligand and downstream signalling molecules were demonstrated.
The 5 clusters identified were – (1) HER-2, HER-3 and phosphoMAPK, (2) NRG3, TGF-α and EGF, (3) Hb-EGF, betacellulin, amphiregulin, NRG1β, NRG 2β, (4) NRG 1α and NRG 4 and (5) EGFR, HER-4, NRG 2α and PTEN. Groups 1, 2 and 5 had significant prognostic significance.

O-106 Preoperative ultrasound and fine-needle aspiration cytology for axillary staging in breast cancer

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Assessment of axillary lymph nodes is very important in patients with breast cancer. Axillary staging is traditionally performed by means of axillary node dissection. But now, it is more important to determine preoperative axillary nodal status. Ultrasonography (US) is the most useful method. The ultrasound-guided fine-needle aspiration cytology(US-FNAC), which is easy to access to suspicious-appearing lymph nodes, provides additional advantages to this modality. The purpose of this study was to assess the accuracy of US and US-FNAC in the preoperative diagnosis of metastatic invasion of the axilla in patients with breast carcinoma. Between May 2005 and April 2006, axillary US was performed in 189 patients with breast cancer and in 84 patients US-FNAC was done. Lymph nodes were classified as benign, suspicious, or malignant. US-FNAC was performed on lymph nodes sonographically suspicious/malignant or bigger than 1.0 cm. US-FNAC established axillary metastases in 29 of the 189 patients. These 29 were 48% of the 61 patients proven to have axillary metastases in final histology. The sensitivity, specificity, positive and negative predictive value of US alone were 54, 91, 75 and 81%, while in US-FNAC, the respective values were 82, 96, 97 and 81%. Preoperative axillary US in a combination with US-FNAC