

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 $85\pm 9\%$ and $70\pm 5\%$ 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 Pearson's 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 were 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, NRG1 β , NRG 2 β , (4) NRG 1 α and NRG 4 and (5) EGFR, HER-4, NRG 2 α 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 1.0cm. 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

is a simple, minimally invasive, and reliable technique for the initial determination of axillary lymph node status in patients with breast cancer.

O-107 The role of axillary ultrasound (US) and fine needle aspiration cytology (FNAC) as pre-operative axillary staging procedure in patients with operable breast cancer

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Introduction: Sentinel Lymph Node Biopsy (SLNB) is the axillary staging procedure of choice in patients with operable breast cancer. However, patients with positive sentinel lymph nodes require further treatment by either axillary node clearance (ANC) or radiotherapy. The role of axillary ultrasound (US) and fine needle aspiration cytology (FNAC) in selecting patients for SLNB or ANC remains unclear.

Methods: A prospective cohort study was undertaken to assess the role of axillary US and FNAC in patients with operable breast cancer. Between October 2005 and September 2006, 100 patients with operable breast tumours and no clinically palpable axillary nodes were examined by axillary US. 24 patients with enlarged or 'malignant' nodes also underwent axillary FNAC.

Results: Overall, 44 patients had US and/or FNAC evidence of axillary nodal involvement. Only one patient with definite US evidence of nodal involvement had a negative ANC. The sensitivity and specificity of US and FNAC in determining nodal involvement were 64% and 70%; 77% and 100% respectively. In the absence of pre-operative US and FNAC, SLNB would have been inappropriate in 32% of patients. With the help of axillary US and FNAC, only 11% of SLNB procedures yielded positive nodes.

Conclusions: Axillary US and FNAC of suspicious nodes should be included in investigation of patients with operable breast cancer. It assists in the selection of the most appropriate axillary staging procedure and may reduce the rate of positive sentinel nodes.

O-108 Ultrasound scan monitoring of response to neoadjuvant chemotherapy in early breast cancer: good predictor for success of breast conservation surgery, but correlates poorly with final histology size

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Introduction: This study was conducted to assess accuracy of ultrasound scan (USS) in determining size of residual breast tumour during and after neoadjuvant chemotherapy (NC) and the likelihood of achieving breast conservation surgery (BCS).

Methods: In this retrospective study over 4 year period, 61 women with large operable breast cancers ($T_{2-4}N_{0-2}M_0$), unsuitable for BCS, were consecutively treated with NC (FEC + Taxotere) at Chase Farm Hospital. Response was monitored clinically and radiologically (USS) during the course of treatment and compared with final pathology.

Results: BCS was achieved in 48 (79%) patients. Reasons for failure of BCS were cancer progression in 2 patients, involved resection margins in 6, multi-focal disease in 3 and patient choice in 2. USS size, when compared to final histology size was accurate (within -3 to +3mm) in only 19 (31%) patients. USS under-estimated the size in 32 (53%) patients. The under-estimation was 4–7 mm in 15 (25%) and 8–24 mm in 17 (28%) patients. USS over-estimated the tumour size by more than 3 mm (3–15 mm)

in 10 (16%) patients. Clinical response (seen in 90% patients) was predictive of successful conservation in 84% whereas radiological response (80% patients) correlated with successful outcome in 90%.

Conclusion: Although USS does not correlate well with the final histopathological size of the breast tumour, it is a sensitive predictor of response to NC & the final outcome i.e. breast conservation. However, the fact that it under-estimates the size should be borne in mind when planning breast conservation after NC.

O-109 Is early response a useful predictive factor in neoadjuvant chemotherapy

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Aim of study: To determine whether response after 2–3 cycles of neoadjuvant chemotherapy correlates with histopathological response obtained after completion of neoadjuvant chemotherapy. Contrast enhanced MRI was the imaging tool used in this study.

Methods: Women with histologically proven breast cancer with a tumour size ≥ 2 cms were considered for neoadjuvant chemotherapy. Using a prospectively maintained database we identified 77 women with 78 breast cancers who underwent neoadjuvant chemotherapy between 2002–2004. Prior to commencing chemotherapy all patients had gadolinium enhanced MRI of breasts. Tumour bulk, extent and activity were measured on MRI. Patients were started on a combination chemotherapy using FEC-75. After 2 cycles, MRI was repeated and response assessed. A response score between -1 (progression) and +4 (complete response) was given to each patient. Responders continued with the same chemotherapy. The minimal/non-responders continued on the same regimen or were switched to a taxane. All patients underwent lumpectomy or mastectomy with level-II axillary clearance after six cycles of chemotherapy. ER+ patients were commenced on appropriate endocrine therapy. They also received post-operative loco regional radiotherapy as per unit guidelines.

Results: Median age was 44.5 years. Median baseline tumour size was 5 cm. pCR was obtained in 13 patients. (16.5%) 12 of these patients scored 2 or 3 on 2nd MRI. Of the 51 patients who had a lower score on interim MRI, 1 achieved pCR when switched to alternative chemotherapy. In our study we found small tumour size and ER negativity predicted for pCR. Survival data will be presented.

Conclusions: Early response in neoadjuvant chemotherapy seems to be a predictor for complete pathological response. MRI reliably identifies early responders in neoadjuvant chemotherapy.

O-110 The challenges of using radiological 'tumour response' as an endpoint in Neo-tAnGo: a national neo-adjuvant chemotherapy breast cancer trial

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When designing a neo-adjuvant clinical trial with radiological 'tumour response' as an endpoint, specifications/recommendations are required in the trial protocol regarding the appropriate scanning techniques and format for reporting findings on the case record forms. The type of radiological scan and number of recorded dimensions of a tumour may vary, not only across hospitals but also within-hospitals across patients or assessment times. An additional issue is whether response on all existing or