Conclusions: OSNA is a promising new molecular technique for rapid examination of SLNs in BC patients. The second phase of this study will investigate the efficiency of OSNA as an intra-operative diagnostic tool.

O-43 Global histone modifications in breast cancer tissue correlate with tumor phenotype, prognostic factors and patient outcome

S. El-Sheikh*, A.R. Green, E.A. Rakha, R.A. Ahmed, E.C. Pais, M.J. Grainge, G.R. Ball, J.F. Robertson, D.M. Heery, I.O. Ellis. *University of Nottingham, UK*

Background: Epigenetic changes in the form of global histone modification patterns have recently been shown to predict patient outcome in human prostatic carcinoma. However, the clinical significance of these modifications in breast cancer is unknown.
Methods: Seven specific antibodies were used to detect selected histone modifications in tissue microarrays of a large (n = 880) well-characterized series of human breast carcinomas using blinded semiquantitative scoring, in addition a set of well known markers in breast cancer.
Results: There is a highly significant correlation of histone modification status with tumor biological/morphological characteristics and clinical outcome. High levels of histone modifications were detected in luminal steroid receptor positive tumours, including lobular, mucinous and tubular carcinomas. However, significantly reduced levels of histone lysine acetylation (H3K9, H3K18, H4K12, H4K20), lysine methylation (H3K4, H4K16) and arginine methylation (H4R3) were observed in the poorer prognostic biological and morphological subtypes of breast cancer including basal and HER2-positive carcinomas, invasive duct carcinoma and medullary-type carcinoma. Low levels of these epigenetic marks were also associated with shorter disease free interval (DFI) and overall survival (OAS), particularly AcH3K18 that has an independent prognostic influence.
Conclusions: Our results show, for the first time, that global changes in specific histone modifications patterns may play an important role in breast cancer development and progression and their reduced expression is associated with poor prognosis and shorter survival.

O-44 Evaluation of estrogen and progesterone receptor, Her-2 and Topo IIα in primary breast cancer and metastatic axillary lymph nodes

B. Ataseven*, D. Michler, B. Hoegel, M. Beer, W. Eiermann. *Red Cross Womens Hospital, Munich, Germany*

Background: Systemic treatment of breast cancer depends on different criteria, e.g. tumor size, grading, receptor status, Her-2/neu-Score. Usually these determinators are carried out using primary tumor tissue based on the assumption that the markers do not change during metastatic progression. We studied the concordance of estrogen (ER) and porgesterone receptor (PR), Her-2 and Topo IIα in primary breast cancer tissue and lymph node metastases.
Methods: We used paraffin-embedded tumor tissue from 118 patients with at least one ipsilateral metastatic lymph node. Immunhistochemistry (IHC) was used to analyze ER, PR, Her-2 and Topo IIα in primary tumor and lymph node. In Addition, Her-2 and Topo IIα amplification was evaluated by Fluorescence In Situ Hybridization (FISH) and Chromogenic In Situ Hybridization (CISH) in all samples with HER-2 Score 2+/3+ by IHC.
Results: Discordant results were seen in 2.56% (ER), 3.45% (PR), 3.42% (Her-2), 3.45% (Topo IIα) by IHC, respectively. However, using FISH and CISH, we found a complete concordance (100%) of the Topo IIα and HER-2 gene status between the primary tumor and the corresponding axillary lymph node. Comparing FISH and CISH, our results show a higher sensitivity with CISH detecting amplification of Topo IIα, whereas there was no difference in the detection of HER-2.
Conclusions: High concordance (approximately 96%) between primary tumor and metastatic lymph nodes of the examined biological markers was detected by Immunhistochemistry, and complete (100%) concordance using FISH and CISH. Nevertheless we recommend routine determination of Her-2 at metastatic lymph nodes, in order to treat all patients with Her-2 overexpression with trastuzumab. Regarding our results, HER-2 testing should be done with FISH, and Topo IIα should be detected by CISH, in order to obtain the highest sensitivity.

O-45 Reproducibility and interpretation of quantitative gene expression measurements in breast cancer biopsies

A. Larionov*, E. Murray, W.R. Miller, J.M. Dixon. *Edinburgh Breast Research Group, UK*

Background and Objectives: Interpretation of genetic signatures on individual clinical specimens is needed to introduce quantitative gene expression measurements into clinical practice. In present study we measured mRNA expression of selected genes in homogenates of core biopsies to (i) evaluate the reproducibility of qPCR measurements in paired biopsies from the same tumour, (ii) to correlate measurements performed using qPCR and micro-array and (iii) to compare different ways of results representation.
Methods and Results: Repeatability of qPCR measurements in paired biopsies taken from the same tumour was studied for CCNB1 and MGB1 genes. Correlations between micro-array measurements and qPCR were studied for CCNB1, CDC2, NUSAP1, COLEC12, DCN, MMP2 and Ki67 genes. Relative coefficients of repeatability in qPCR were 2.2 and 15 fold for CCNB1 and MGB1 correspondingly. Exclusion of obvious outliners improved the coefficients of repeatability to 1.3 and 3.1 fold correspondingly. Positive correlations ($p < 0.001$) were observed between qPCR and micro-arrays for all studied genes except Ki67. Binary classification (ROC plots) and probability calculation (logistic regression) were compared to represent the outcomes of multi-gene quantitative measurements for interpretation.
Conclusions: (1) Paired biopsies taken from the same tumours may be used to validate quantitative gene expression measurements and possibility of their individual interpretation. (2) Representing results in the form of probability reflects the status of quantitative mRNA expression measurements better than presenting results as a discrete classification.

O-46 The prognosis of small breast cancers and selection for omission of adjuvant chemotherapy

M. Sundquist*, M. Mitchell, R. Blamey, M. Blichert-Toft, L. Cataliotti, K. Holli, R. Jakesz, M. Kerin, I. Monypenny, M. van de Vijver, B. Hornmark-Stenstam, T. Pienkowski, On behalf of the ONCOPOOL Consortium

Aim: To recognise those cancers with excellent survival without adjuvant systemic therapy. Various studies have advanced criteria eg. all <10 mm (or) ⩽10 mm, LN neg, LVI neg, grade I.
Patients and methods: ONCOPOOL collected data from 16,893 operable (<5 cm) breast cancers aged 29–70 years, consecutively diagnosed in periods within 1990–99 at 13 European Breast centres. Women who received