13%), tumor size (T1 59% T2 39% T3 1.6%) and grade (G1 32% G2 39% G3 15%).
Results: Median follow-up was 47 months. Actuarial (OS and DFS) at 4 years were luminal A (99.3% and 95.8%), luminal B (95.6% and 80.4%), Her2 (89.8% and 80.9%) and triple negative (74.6% and 58.7%), p = 0.0001; for N0 (98.8% and 93.9%) N1−3 (90.8% and 83.6%) and N > 4 (87.1% and 71.8%), p = 0.0001. Significant independent prognostic factor for OS were BC subtypes (with relative risk (RR) luminal B 4.7, Her2 3.6 and triple negative 12.08 referent to luminal A, p = 0.0001), and the number of positive nodes (N1−3 RR = 6.6 and N > 4 8.3 referent to N0 category, p = 0.004), respectively. Significant independent prognostic factor for DFS were BC subtypes (with relative risk (RR) luminal B 4.8, Her2 3.9 and triple negative 7.7 referent to luminal A, p = 0.0001), the number of positive nodes >4 (RR 2.01 referent to N0 category, p = 0.049) and tumor size (T2 RR 2.28 referent to T1 category, p = 0.004).
Conclusions: A simple immunopanel can divide breast cancers into biologic subtypes with independent prognostic effects and provides additional information to nodal status. Triple negative status emerged as a strong adverse prognostic factor.

5163 POSTER

Methylation in breast cancer and correlate ER with tumor phenotypes and prognostic factors

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Background: To investigate the association between ESR1 gene hypermethylation and tumor phenotype including diagnosis and treatment response are the objetive of this studies. Other gene as 14−3-3σ were also analized.
Materials and Methods: Since January 2002 to June 2005, 107 women with breast cancer and 108 control subjects were recruited. Real Time QMS-PCR SYBR green (methylation-specific PCR) was used to analyze the methylation of *ESR1* and *14−3-3σ* gene promoter regions as breast cancer biomarkers. Tumours were classified as phenotype basal, luminal A, Luminal B and phenotype HER2+.
Results: Ours analyses revealed low or absent methylation *ESR1*and *14−3-3σ* in healthy controls and significant differences between breast cancer patients (pts) and healthy controls in relative serum levels of methylated gene promoters *ESR1 (p* = 0.0112) and *14−3-3*s (p = 0.0047). Presence of methylated *ESR1* in serum of breast cancer patients was associated with *ER-negative* phenotype (*p* = 0.0179). Of the available cases, 60 pts (56%) were Luminal A, 10 pts (9.3%) Luminal B, 13 pts (12%) Basal like and 9 pts (8.4%) HER2+. We observed that methylated *ERS1* was preferably associated with phenotype Basal Like and worse interval progression free and survival global though p > 0.05. We observed that hypermethylation of *ERS1* and *14−3-3σ* combined differentiated between breast cancer patients and healthy controls (p = 0.0001) with a sensitivity of 81% (95% CI: 72−88%) and specificity of 88% (95% CI: 78−94%). In addition observed lower methylated *ERS1* and *14−3-3σ* value after surgery, respect pretreatment levels, but without an overall statistically significant difference. With a median follow up of 6 years, we found that patients with a significant decrease of sera methylated levels of both genes after surgery had better time to progression an overall survival respect patients without this observation.
Conclusions: This study identifies the presence of variations in global levels of methylation promoters genes in healthy controls and breast cancer with different phenotype classes and shows that these differences have clinical significance. In the future this panel of genes detected could be useful as markers for early detection of breast carcinoma. These findings cast some doubts on the utility for early cancer diagnosis of highly sensitive techniques to identify hypermethylation of specific gene promoters in DNA extracted from serum. Although numerous issues remain to be resolved, the quantitative measurement of circulating methylated DNA is a promising tool for cancer risk assessment.

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Impaired glucose tolerance in non-diabetic women during adjuvant chemotherapy for breast cancer

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Background: Up to 16% of patients with breast cancer have diabetes and diabetic individuals tend to have poorer outcomes following treatment for breast cancer. During chemotherapy, dexamethasone is widely used to prevent side effects. However, glucocorticoid administration is associated with impairment of insulin sensitivity, elevations in peripheral glucose levels as well as suppression of the hypothalamic-pituitary-adrenal axis for up to 3 weeks. We measured blood glucose levels in a group of non-diabetic women receiving adjuvant chemotherapy for breast cancer.
Materials and Methods: 39 women (age 58.6±12.8 years, BMI 27.2 +/-4.9 kg/m^2) participated in this study which was approved by the local ethics committee and all patients gave informed consent. Patients received either 6 cycles of fluorouracil, epirubicin, cyclophosphamide (FEC) (18) or 3 cycles of FEC followed by 3 cycles of docetaxel (21). Before each cycle of FEC, patients received 8 mg of dexamethasone (po). The patients who received docetaxel had 8 mg of dexamethasone (po) 24 hours, 12 hours and immediately before docetaxel. For each cycle of chemotherapy non-fasting glucose was measured before the treatment cycle began, immediately after the pre-chemotherapy Dexamethasone was administered but before chemotherapy and, immediately after chemotherapy and 10 days after each cycle.
Results: There was an increase in blood glucose levels with later cycles among women who received the higher dose of Dexamethasone in combination with docetaxel (cycle 5: P < 0.001; cycle 6: P = 0.002 [paired *t* tests]) (Table). Before the first cycle of chemotherapy, none had blood glucose levels in either the impaired glucose tolerance range (ie, 7.8−11.1 mmol/L) or the diabetic range (ie, >11.1 mmol/L). Increasing number of patients developed glucose intolerance as cycles progressed; 6 had blood glucose levels in the impaired tolerance range and 8 had levels within the diabetic range following the 5th cycle.

Cycle	Before treatment cycle	Immediately after Dexamethasone but before chemotherapy	After Dexamethasone and chemotherapy	10 d after chemotherapy
1	5.8 [1.1]	4.8 [0.7]	5.7 [2.0]	5.7 [0.7]
2	5.5 [0.9]	5.6 [1.0]	5.5 [0.8]	5.5 [1.0]
3	5.3 [0.9]	5.5 [1.3]	5.9 [1.5]	5.8 [1.4]
4	5.6 [0.9]	6.0 [1.6]	6.4 [1.8]	5.6 [0.8]
5	5.3 [1.0]	7.7 [3.0]	7.8 [2.7]	6.0 [2.0]
6	5.5 [0.8]	8.0 [2.7]	8.1 [3.1]	6.0 [1.2]

Conclusions: The implications of transient hyperglycaemia on the efficacy of chemotherapy in this setting is uncertain and further investigation is indicated.

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Microarray based determination of ER, PR and HER2 receptor status compared to local IHC assessment in 11 hospitals

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Background: The level of estrogen receptor (ER), progesterone receptor (PR) and HER2 expression is predictive for prognosis and/or treatment response in breast cancer patients. However, differences in immunohistochemistry (IHC) methods and interpretation can substantially affect the accuracy and reproducibility of the results. The recently developed TargetPrint test measures the mRNA expression level of ER, PR and HER2 and provides an objective alternative to IHC. This study describes a