

**Patients and Methods:** Data regarding a series of 255 consecutive women (median age 60 years, range 30-85) with pT1-2 (pT1a=9, 3.5%; pT1b=38, 14.9%; pT1c=107, 42.0%; pT2=101, 39.6%) BC were reviewed, while patients with confirmed pT3-4 BC were excluded. The greatest diameter of the tumor measured by the pathologist (size) ranged from 3 and 48 mm (median 19 mm). There were 71 (27.8%) premenopausal and 184 (72.2%) postmenopausal women. Two groups of patients were considered according to the axillary lymph node status: Group A, 70 (27.5%) cases (pN1), and Group B, 185 (72.5%) cases (pN0). All patients underwent preoperative CEA and CA 15-3 serum levels measurement, and the removed tissue was routinely processed for the detection of ER, PgR, and MIB1 index.

**Results:** CEA and CA 15-3 serum levels were above the cut-off (10 ng/mL, and 30 U/L, respectively) in 44 (17.2%) and 75 (29.0%) patients (Group A: 22.9% and 47.0%, Group B: 15.1% and 23.0%, respectively; p=NS). Size ( $23.9 \pm 9.0$  vs.  $18.2 \pm 9.3$  mm), ER rate ( $51.3 \pm 37.7$  vs.  $60.4 \pm 30.6$ ), MIB1 index ( $30.1 \pm 26.3$  vs.  $17.8 \pm 21.0$ ), CEA ( $4.3 \pm 4.8$  vs.  $3.4 \pm 2.7$  ng/mL) and CA 15-3 ( $26.8 \pm 16.3$  vs.  $18.2 \pm 15.1$  U/L) serum levels were significantly different ( $p < 0.05$ ) in Groups A and B patients. Overall, a significant correlation between size of the tumor and both CEA ( $R=0.22$ ,  $p=0.0003$ ) and CA 15-3 ( $R=0.57$ ,  $p < 0.0001$ ) and between ER rate and MIB1 index ( $R=0.59$ ,  $p < 0.0001$ ) was found. There was no relationship between age of the patients, size ( $R=0.08$ ,  $p=0.20$ ), and ER ( $R=0.13$ ,  $p=0.71$ ). Among Group A patients, a significant correlation between number of involved nodes and both CEA ( $R=0.24$ ,  $p=0.04$ ) and CA 15-3 ( $R=0.31$ ,  $p=0.007$ ) serum levels was found, but there was no relationship ( $p=NS$ ) with age, ER rate and MIB1 index.

**Conclusions:** In patients with BC, serum markers CEA and CA 15-3 correlate exclusively with the size of the tumor. On account of their low sensitivity and in lack of relationship with others prognostic factors, preoperative CEA and CA 15-3 serum levels measurements are of little value in patients undergoing curative surgery for primary BC.

420

POSTER

### Predictive factors for the status of non-sentinel nodes in breast cancer patients with tumor positive sentinel nodes

V. van Iterson<sup>1</sup>, M.H.K. Leidenius<sup>1</sup>, L.A. Krogerus<sup>2</sup>, K.J.A. von Smitten<sup>1</sup>.

<sup>1</sup>Breast Surgery Unit, <sup>2</sup>Department of Pathology, Maria Hospital, Helsinki University Hospital, Helsinki, Finland

**Background:** In breast cancer patients with tumor negative sentinel nodes axillary lymph node dissection is omitted and the patient spared from postoperative morbidities. However in patients with tumor positive sentinel nodes, axillary lymph node dissection is routinely performed while a majority of these patients have no tumor involvement in the non-sentinel nodes. The authors tried to identify a subgroup of patients with a tumor positive sentinel node without non-sentinel node tumor involvement.

**Methods:** In 135 consecutive patients with clinical stage T1-T2 node-negative breast cancer, tumor positive sentinel nodes and axillary lymph node dissection performed, the incidence of non-sentinel node involvement according to tumor and sentinel node related factors was examined.

**Results:** The size of the sentinel node metastasis, size of primary tumor and number of tumor positive sentinel nodes were the three factors significantly predicting the status of the non-sentinel nodes. The size of the sentinel node metastasis was the strongest predictive factor ( $P < 0.0001$ ). In a subgroup of 41 patients with a stage T1 tumor and micrometastatic involvement in the sentinel node only 2 patients (5%) had non-sentinel node involvement.

**Conclusion:** In patients with small primary tumors and micrometastatic involvement of the sentinel nodes, the chance of non-sentinel node involvement is small but can not be discarded. Because the clinical relevance of micrometastases in lymph nodes is still unclear it is not advisable to omit axillary lymph node dissection even in these patients.

421

POSTER

### Expression of estrogen receptor- $\beta$ 2 and $\beta$ 4 mRNA decreases in breast carcinogenesis

B.-W. Park<sup>1</sup>, K. Kim<sup>2</sup>, M. Heo<sup>2</sup>, W. Yang<sup>3</sup>, J. Kim<sup>4</sup>. <sup>1</sup>Surgery, <sup>2</sup>Brain Korea 21 Project, <sup>3</sup>Pathology, <sup>4</sup>Internal Medicine, Yonsei University College Of Medicine, Seoul, Korea

**Background:** Since the discovery of estrogen receptor- $\alpha$  (ER $\alpha$ ), more than five variants have been identified. There have been many controversial reports on the role of ER $\alpha$  in breast carcinogenesis and cancer progression, and its prognostic implications. The role of the variant forms has not been yet identified.

**Materials and Methods:** Using reverse transcription polymerase chain reaction (RT-PCR), we examined the expression levels of ER $\alpha$  and ER $\beta$  variants in 76 paired normal and cancer tissues, 6 paired normal and benign tumor tissues, and 12 metastatic lymph nodes. We compare the densities of RT-PCR products using Tina version 2.10 (Raytest, Germany). Chi-square test and independent t-test were used for the statistical analysis. Differences were considered significant with a p value of less than 5%.

**Results:** ER $\alpha$  expression was increased in 51 cancer tissues (67.1%) compared to matched normal tissues and decreased only in 9 (11.8%). On the contrary ER $\beta$  expression was decreased in 42 cancers (55.3%) compared to matched normal tissues and increased only in 4 cancers (5.3%). Among ER $\beta$  variants, ER $\beta$ 2 was predominant and expressed 100% in both normal and cancer tissues but the level of expression decreased significantly in cancers compared to paired normal tissues. ER $\beta$ 4 was also expressed in both normal and cancer tissues 77.6% and 73.6%, respectively and it decreased significantly in cancer tissues compared to paired normal tissue, too. ER $\beta$ 5 was expressed more frequently in cancer tissue (57.9%) than in normal tissue (31.7%). ER $\beta$ 1 expression was not significantly different between normal and cancer tissues. There was no ER $\beta$ 3 expression in both normal and cancer tissues.

**Conclusions:** Among ER $\beta$  variant forms, ER $\beta$ 2 is predominant in both normal and cancerous mammary tissues and ER $\beta$ 4, ER $\beta$ 5, and ER $\beta$ 1 in descending order but ER $\beta$ 3 is not expressed in the mammary tissue. ER $\beta$  mRNA expression significantly increases but ER $\alpha$  mRNA decreases in the process of breast cancer development and progression. The decrease of ER $\beta$ 2 and ER $\beta$ 4 expression is a dominant phenomenon during the breast carcinogenesis, which suggests that ER $\beta$ 2 and ER $\beta$ 4 may possess a regulatory function of mammary proliferation. Further investigations to verify the roles of ER $\beta$  variants are mandatory.

422

POSTER

### Soluble adhesion molecules and oxidative stress in patients with breast cancer

P. Tesarova<sup>1</sup>, M. Kalousova<sup>2</sup>, T. Zima<sup>2</sup>, E. Helmichova<sup>1</sup>, K. Trskova<sup>1</sup>, L. Petruzelka<sup>1</sup>. <sup>1</sup>Department of Oncology, <sup>2</sup>Department of Clinical Biochemistry, Charles University, Prague, Czech Republic

**Background:** Identification of clinically useful prognostic markers and markers of activity could contribute to the improvement of therapy of patients with breast cancer, mainly to the identification of subgroups of patients in higher risk of the formation of metastases and early detection of relapses of the disease. In patients with breast cancer oxidative stress may modify membrane lipids which may then become the target of some autoantibodies. Some receptors (including EGF receptor and apo1/Fas) and adhesion molecules (standard and/or variant CD44 and P-selectin) may detach from the surface of tumor cells and increased levels of their soluble forms may be also identified in sera.

**Methods:** In our study serum levels of soluble EGF receptor, soluble standard and variant CD44 (CD44s and CD44v6, respectively), soluble P-selectin, soluble apo-1/Fas, advanced oxidation protein products (AOPP), advanced glycation end-products (AGEs), pregnancy associated plasma protein (PAPP-A) and IgG and IgM anticardiolipin antibodies (ACA) were studied in 76 patients (pts) with newly diagnosed, mostly non-metastatic breast cancer (3 pts in stage 0, 37 pts in stage I, 18 pts in stage IIA, 12 pts in stage IIB, 4 pts in stage III and 2 pts in stage IV) and compared with 8 age-matched healthy women.

**Results:** Patients with breast cancer had significantly higher serum levels of soluble standard form of CD44 (CD44s,  $581.5 \pm 281.1$ , vs.  $406.4 \pm 48.9$  ng/ml,  $p < 0.05$ ), but not soluble variant form, most common on breast cancer cells (CD44v6,  $171.4 \pm 48.4$  vs.  $160.1 \pm 48.3$  ng/ml,  $p = n.s.$ ). Serum levels of soluble P-selectin ( $248.1 \pm 137.0$  vs.  $125.5 \pm 32.0$  ng/ml,  $p < 0.05$ ) and serum levels of soluble apo-1/Fas ( $852.9 \pm 159.3$  vs.  $541.5 \pm 124.5$  pg/ml,  $p < 0.05$ ) were also significantly increased in patients with breast cancer. Concerning the markers of oxidative stress patients with breast cancer had higher AOPP ( $93.6 \pm 46.8$  vs.  $68.5 \pm 23.1$   $\mu$ mol/l,  $p < 0.05$ ), but there was no difference in AGEs, PAPP-A and IgM and IgG ACA. We were not able to find any significant difference in serum levels of soluble EGF receptor ( $3.2 \pm 3.1$  vs.  $3.6 \pm 2.0$  ng/ml,  $p = n.s.$ ). None of measured parameters was able to discriminate the patients with different stages of breast cancer.

**Conclusions:** Patients with breast cancer (including those in early stages of the disease) may have increased serum levels of some soluble adhesion molecules (sCD44s, sP-selectin), markers of apoptosis (sapo-1/Fas) and oxidative stress (AOPP). Further follow-up should demonstrate the response of these markers to hormonal therapy/chemotherapy and putative prognostic significance of increased levels of these markers in order to improve the current possibilities to monitor the activity of the disease and to predict its