

TRAIL and TRAIL receptor expression was investigated in breast cancer patients with invasive ductal carcinoma.

**Methods and Materials:** Patients were selected from a cohort of 133 consecutive patients with nonmetastatic invasive ductal carcinoma treated at the Department of Radiation Oncology at the Akdeniz University Faculty of Medicine. Of these 133 patients, 90 (67.6%) had paraffin-embedded breast cancer tissue samples available for examination and immunohistochemical staining, and for subsequent evaluation in terms of various characteristics, including age, menopausal status, tumor size, axillary lymph node involvement, histological grade, lymphovascular invasion (LVI), perineural invasion, extracapsular extension (ECE), presence of an extensive intraductal component (EIC), multicentricity, estrogen and progesterone receptor status, *CerbB2* (*HER2/neu*) oncogene status, and adjuvant radiotherapy and/or systemic treatment. Of these patients, 25 patients (27.7%) were treated with breast-conserving surgery (BCS), and 65 patients (72.2%) were treated with modified radical mastectomy and level I-II axillary dissection. All patients underwent postoperative external beam radiation therapy (RT) as a component of their treatment.

**Results:** DR4 expression was significantly higher compared to TRAIL, DR5, *DCR1*, and *DCR2* expression. While progesterone receptor positive patients exhibited lower DR5 expression, *CerbB2* positive tissues displayed higher levels of both DR5 and TRAIL expressions.

**Conclusions:** DR4 was the highest TRAIL receptor expressed in patients with invasive ductal carcinoma. DR4 expression might be important for the transition from a low grade to a high grade tumor.

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POSTER

#### Post-mastectomy breast reconstruction complications – ten years experience

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**Background:** Complications of reconstructive procedures after mastectomy are divided into early (infection) and late (endoprosthesis prolapse, capsular contracture, iatrogenic damage of endoprosthesis, local recurrence). Skin flap necrosis or musculo-cutaneous lobe necrosis can be both early and late complication and it occurs as sequela of compromised vascularization or influence of certain factors (radiotherapy, infection).

**Materials and Methods:** During 1997 and 2006, 682 reconstructive procedures in 593 patients were performed at Institute of Oncology and Radiology of Serbia. Primary reconstruction was performed in 484 (71%) cases, postponed reconstruction in 109 (16%) cases and correction of healthy breasts because of symmetrization in 89 (13%) cases. From 484 primary reconstructions, 376 were positioned subpectorally, 104 subcutaneously, while 2 of them were performed as a combination of endoprosthesis and *m. latissimus dorsi* flap. Postponed reconstructions were performed in 72 cases by implanting endoprosthesis, in 30 cases by combining *latissimus dorsi* musculo-cutaneous flap and endoprosthesis and in 7 cases TRAM method was used. Most of the patients were treated with postoperative adjuvant chemotherapy and some of them with combined radio chemotherapy too.

**Results:** Out of 682 reconstructive operational procedures, complications occurred in 66 (9.7%) cases (28 prostheses prolapses, 26 in primary reconstructions and 2 in postponed). Capsular contracture occurred in 26 (3.8%) (25 after primary reconstruction and 1 after postponed reconstruction). Other complications, which were 12 (1.8%), occurred in 10 cases (infection), in one case (iatrogenic damage of endoprosthesis) and in one case (pseudo cyst). Prolapse of primary reconstructions occurred in 10 (2.7%) cases of subpectorally positioned endoprosthesis and in 16 (15.4%) cases of subcutaneously positioned endoprosthesis. Out of 26 prolapses of primary reconstructions in 3 cases the cause was post operational chemotherapy, adjuvant chemotherapy in 4 cases, skin necrosis in 15 cases, and among 4 women the rejection of implant occurred.

**Conclusion:** Number of complications is smaller if the implant is positioned subpectorally. Post operational radio and chemotherapy increase the risk of complications. Number of complications was reduced as the operational technique improved which shows that operational skill is an important factor for complications occurrence.

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POSTER

#### Age-related methylation pattern of ESR1 in patients with breast cancer

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**Background:** The methylation of some genes increases or decreases as acquired with age in different tissues. These age-dependent methylation changes of some genes can have pathologic processes and causing to

the progressive growth of tumor. The purpose of this study was to evaluate the effects of aging on the methylation of specific genes in breast cancer.

**Materials and Methods:** Thirty-nine paired samples of human breast cancer and adjacent normal tissues were collected. The breast cancer tissue was performed immunohistochemical staining for ESR1, PgR, HER-2 and P53. Genomic DNA from paired cancer and normal tissues were isolated. To perform bisulfite sequencing analysis of ESR1, PgR, RASSF1A, CDH13 and CYP 1B1, 25 ng of bisulfite-modified DNA was amplified with primer sets which were designed using MethPrimer program. PCR products were randomly chosen for sequencing. Three CpG sites in the 5'-upstream region of genes were selected for quantitation of methylation. Bisulfite-modified DNA was amplified by PCR; the PCR was modified for pyrosequencing based methylation analysis. Pyrosequencing was completed automatically by using a PSQ HS 96A system (Biotage AB). Methylation patterns of ESR1, PgR, RASSF1A, CDH13 and CYP 1B1 were analyzed according to age above and below 50 years old.

**Results:** Below 50 years old, mean of methylation frequencies of the gene tested in the normal tissue and tumor tissue was 88.29% and 83.23% for ESR1, 3.75% and 5.72% for PgR, 5.45% and 20.94% for RASSF1A, 4.31% and 8.51% for CDH13 and 2.07% and 2.39% for CYP1B1. Above 50 years old, mean of methylation frequencies of the gene tested in the normal tissue and tumor tissue was 87.71% and 74.36% for ESR1, 4.08% and 5.96% for PgR, 7.17% and 19.34% for RASSF1A, 4.26% and 9.53% for CDH13 and 1.75% and 2.44% for CYP1B1. Hypomethylation of ESR1 over the age of 50 years in breast cancer showed strong correlation with age and statistical significance was noted. PgR, RASSF1A and CDH13 showed hypermethylation pattern with aging, but statistical significance was not noted. Hypomethylation of ESR1 showed strong correlation with over the age of 50 years in breast cancer. CYP1B1 does not show methylation change with aging.

**Conclusions:** Hypomethylation of ESR1 in breast cancer showed strong correlation with age. ESR1 expression reflects the change of DNA methylation with age and the methylation related to the aging may contribute to the hypomethylation in breast cancer.

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POSTER

#### Validation of a nomogram to predict the risk of non-sentinel lymph node metastasis in breast cancer patients with a positive sentinel node biopsy

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**Background:** Completion axillary lymph node dissection (ALND) remains, according to the Dutch guidelines, the standard of care for patients with a positive sentinel lymph node (SLN). However, approximately 40–60% of patients with positive SLNs will have no additional positive nodes. To identify the individual patient's risk for non-SLN metastases, the Memorial Sloan-Kettering cancer Center (MSKCC) developed a nomogram currently available as an online tool. The purpose of this study was to validate the nomogram in a Dutch population of breast cancer patients.

**Methods:** The medical records of 193 breast cancer patients who underwent sentinel lymph node biopsy examination and ALND were selected from a prospectively collected database and were reviewed for multiple clinicopathologic variables. A receiver operating characteristic (ROC) curve was drawn and the area under the curve was calculated to assess the discriminative power of the nomogram. Also, data of the index and test populations were compared.

**Results:** The area under the ROC curve was 0.693 (range 0.614–0.773), as compared to 0.76 in the MSKCC study. When the tool was applied solely to macrometastases, the area under the ROC curve was 0.688 (range 0.595–0.781).

**Conclusions:** The MSKCC-nomogram seems to be a useful tool to predict the individual patient's risk for positive axillary non-sentinel lymph nodes in a Dutch population of breast cancer patients. Further analysis, however, has to be performed to identify subgroups, in which the nomogram is even more predictive. Predicting the risk of additional nodal metastases will allow the surgeon and the patient to make an individualized decision regarding the need for completion axillary lymph node dissection.