Results: 1st cohort: 286 patients' files were reviewed. 82% of tumors were node negative. 80 were PR negative and 209 were PR positive. No significant differences existed between the groups with respect to nodal involvement or grade. After a median follow up of 7.24 years (0.78 to 9.5) 8 women with PR negative and 9 women with PR positive tumors experienced disease recurrence (10% vs 4.3%, RR 2.32, p 0.014 by univariant analyses). 33% of patients (5 out of 15) with grade 3 PR negative tumors experienced recurrence.

2nd cohort: 81 PR negative tumors were included. The rate of discordance between IHC and Oncotype Dx for PR expression was 47.3%. Recurrence scores were: 50% intermediate risk, 32.5% low risk and 17.5% high risk. Grade 3 tumors were more likely to be high risk (37.5%) and PR negative by RT PCR (84.6%).

Conclusion: In our hands PR negative tumors carry a worse prognosis when treated by hormonal adjuvant treatment compared with ER/PR positive tumors. We found a high rate of discrepancy between IHC and RT PCR concerning PR expression.

Most PR negative tumors are labeled intermediate risk. The value of the test in this setting is unclear.

310 Poster

Breast Density Change as a Predictive Surrogate of Adjuvant Anti-estrogen Therapy Response in Estrogen Receptor Positive Breast Cancer

J.S. Kim[1], W. Han[1], J.M. You[1], H.C. Shin[1], S.K. Ahn[1], H.G. Moon[1], D.Y. Noh[1], N. Cho[1], W.K. Moon[1], I.A. Park[1]. *[1]Seoul National Universith Hospital, General Surgery, Seoul, Korea*

Background: Mammographic breast density is an established risk factor of breast cancer. Previous studies showed that adjuvant anti-estrogen therapy lowers breast density. We hypothesized that the change of breast density can be a surrogate marker predicting response to anti-estrogen therapy.

Materials and Methods: We analyzed data of 1,542 estrogen receptor positive breast cancer patients who underwent surgery in Seoul National University Hospital between Oct 2003 and Dec 2006. Of them, patient who accomplished at least 2 year of adjuvant hormone therapy (mmg available) were included and total 1065 cases were evaluated. Percent mammographic density (PMD) was evaluated by comparing mammography taken preoperatively and after 8−18months of adjuvant hormone therapy. PMD was measured with Cumulus software 4.0. Factors associated with the change of PMD (dPMD = postPMD − prePMD) were analyzed and recurrence-free survivals were compared with respect to dPMD.

Results: After median follow up of 67.69 months, overall recurrence rate was 7.5% (80/1065). Mean dPMD was 5.92% (−17.22 to 36.87). In a univariate analysis, younger age, tamoxifen use (vs aromatase inhibitor), high prePMD, high histologic grade, positive lymph node, and adjuvant chemotherapy were associated with higher dPMD (p value <0.05). In a multivariate analysis, age <50, high prePMD and adjuvant chemotherapy were significantly associated with higher dPMD (p value <0.05). In a survival analysis, duration of anti-estrogen therapy, size, LN status, high Ki-67, and dPMD were independent factors associated with recurrence-free survival.

Conclusions: PMD change after about 1 year of adjuvant hormone therapy was a significant predictive factor for long term recurrence-free survival in patients with ER-positive breast cancer. Mammographic density change might be used clinically for the prediction of prognosis in patients taking anti-estrogen therapy.

311 Poster

Vitamin D Receptor and Prognosis in Breast Cancer

N. Ditsch[1], D. Mayr[2], B. Toth[3], S. Hasmüller[2], M. Lenhard[2], T. Weissenbacher[4], I. Himsl[2], K. Friese[5], U. Jeschke[4]. *[1]Ludwig-Maximilians-University − Grosshadern, Gynecology and Obstetrics, Munich, Germany; [2]Ludwig-Maximilians-University, Pathology, Munich, Germany; [3]Ruprecht-Karls-University, Gynecological Endocrinology and Fertility, Heidelberg, Germany; [4]Ludwig-Maximilians-University − Maistrasse, Gynecology and Obstetrics, Munich, Germany; [5]Ludwig-Maximilians-University − Grosshadern and Maistrasse, Gynecology and Obstetrics, Munich, Germany*

Background: The Vitamin D receptor (VDR) belongs to the nuclear class II receptor family. It is involved in cell growth and differentiation in healthy and malignant breast tissue through its binding capacity for vitamin D and shows anti-proliferative effects.

Material and Methods: In this study we analyzed VDR (1,25(OH)2D3 receptor) expression and survival in a breast cancer patient cohort of 82 patients. 75/82 (91.5%) patients showed immunohistochemical results after detection of the VDR expression with monoclonal antibodies and the ABC method. Staining results were classified as Immunoreactive Scores (IRS), which were assigned according to Remmele and Stegner. The IRS score was calculated by multiplication of the staining intensity and percentage of cells stained positive. IRS 0−1 was classified as negative/very low, IRS 2−4 as moderate-high and IRS 6−12 as high. Statistical analysis was performed by Spearman's correlation test ($p < 0.05$ significant). Overall survival was analyzed using Kaplan-Meier estimations.

Results: Only 6 patients (8%) had a negative or very low IRS. Moderate IRS values (2−4) were present in 20 patients (26.7%). Most of the patients had a high IRS (49 patients, 65.3%). For survival analysis, data were dichotomized (IRS 0−4: negative to moderate and IRS 6−12: high VDR expression) because of the small number of patients in the IRS 0−1 group. In univariate analysis, VDR expression showed significant differences in progression-free survival (PFS), $p = 0.046$; HR 0.83, 95% CI 0.73–0.94) and overall survival (OS), $p = 0.014$; HR 0.35; 95% CI 0.15–0.81). Patients with high IRS scores showed a significantly better PFS (log rank: $p = 0.037$) and OS ($p = 0.008$) than patients with moderate or negative IRS scores for VDR expression. VDR expression showed a trend towards a correlation with OS ($p = 0.06$; HR 0.39; 95% CI 0.14–1.04), and clearly non-significant correlation to PFS ($p = 0.436$; HR 0.67; 95% CI 0.24−1.9). When analyzed separately, the 3 different IRS groups (IRS 0−1, 2−4 and 6−12) showed significant differences in VDR expression (multivariate analysis for OS: $p = 0.034$, HR 0.45, 95% CI 0.21–0.94).

Discussion: Our data suggest that VDR expression in breast cancer tissue may be of clinical significance, and the results provide evidence that VDR may be a factor with prognostic relevance.

312 Poster

TROP-2 Expression and Mutation in Familiar Breast Cancer

S. Petroni[1], F. Giotta[2], T. Addati[1], M. Asselti[1], O. Popescu[1], B. Pilato[3], A.L. Marzano[1], F. Palma[1], S. Tommasi[3], G. Simone[1]. *[1]Oncology Institute "Giovanni Paolo II", Pathological Anatomy Unit, Bari, Italy; [2]Oncology Institute "Giovanni Paolo II", Clinical Experimental Oncology Unit, Bari, Italy; [3]Oncology Institute "Giovanni Paolo II", Clinical Experimental Oncology Laboratory, Bari, Italy*

Background: TROP-2 is a transmembrane calcium signal transducer, involved in the regulation of cell-cell adhesion. It is a stimulator of human cancer growth and a marker of metastatic tumor, so it could be a target of diagnostic and therapeutic procedures.

The aim of this study was to analyze TROP-2 expression in two different subset of familiar tumors (patients were selected to have BRCA mutation), to identify patients with a worst outcome disease.

Materials and Methods: We analyzed 32 Ductal Invasive Breast Cancer (CDI), 16 were defined Triple Negative (TN), whereas 16 were Non-Triple Negative (NTN) CDI. All cases were tested for BRCA mutations, TROP-2 mutations and expression, hormonal receptor status (ER, PgR), Ki-67, ck5/6 and EGF-R expression.

BRCA 1/2 and TROP-2 mutations were screened by direct sequencing.

Results: All 16 TN cases had a high proliferation index with an average of 50% (from 25% to 90%), 12 out of 16 samples were negative to ck 5/6 expression, whereas 10/16 were negative to EGF-R reaction.

Moreover, TROP-2 immunoreactivity high or moderate was detected in 6 (37.5%) out of 16 TN breast samples, whereas 10 (62.5%) case had low TROP-2 IR. 5 out of 6 cases with high/moderate TROP-2 score resulted also ck5/6 negative and 4 were EGF-R+. The follow-up data (mean FU: 50.4 months; range: 24–132 months) of these 6 patients revealed that in 5 cases there was disease relapse.

Only 8 out of 16 NTN breast cancer showed a high ki-67 proliferation index with an average of 46% (from 2% to 80%), 12 out of 16 samples were negative to ck 5/6 expression and 6 were EGF-R +. A high and moderate TROP-2 immunoreactivity was detected in 6 (37.5%) out of 16 NTN breast samples, whereas 10 had low IR. 5 out of 6 cases with high/moderate TROP-2 score resulted also ck5/6− and EGF-R−. The follow-up data (mean FU: 40 months; range: 12−72 months) of these 6 patients revealed that in 3 cases there was disease relapse.

Our results show that 8 (67%) out of 12 tumor with TROP-2+ had disease relapse.

As expected, cases with TROP-2 protein overexpression did not presented gene mutations with the exception of 2 cases.

Conclusions: Our data suggest that: (1) there is not difference in TROP-2 expression between TN (37.5%) and NTN (37.5%) familiar breast cancer and (2) TROP-2 positive tumor do not express ck 5/6. TROP-2 overexpression could be predictive for poor disease-free survival and useful as an immunohistochemical prognostic factor related to tumor progression.