prognosis (similar to grade 1) and one with a bad prognosis (similar to grade 3). We therefore also raised the question if a single proliferative factor, i.e. cyclin A, can be used for this purpose.

Material and Methods: In 219 consecutive premenopausal node negative patients, cyclin A was determined with immunohistochemistry on tissue microarray. High cyclin A was defined as the 7th decile of positive cells. Only 13% of the patients received adjuvant systemic therapy. Cox proportional hazards regression was used to model the impact of the prognostic factors on distant disease-free survival (DDFS). Due to non-proportional hazards, the analysis was restricted to the first five years after diagnosis, a time period during which 34 patients developed distant recurrences.

Results: Cyclin A was associated to DDFS in univariate analysis (hazard ratio (HR) 3.6, 95% confidence interval (CI): 1.8−7.1, $p < 0.001$). Corresponding HR:s were 2.7 for Ki67 (95% CI: 1.3−5.5, $p = 0.005$) and 2.7 for grade 3 *vs* 1+2 (95% CI: 1.3−5.2, $p = 0.004$). HER2, age, ER and progesterone receptor were also significant factors, whereas tumor size was not. Cyclin A could divide histological grade 2 into two groups with significantly different DDFS (HR: 15, 95% CI: 4.3−52, $p < 0.001$). In the grade 1 and 3 subgroups, cyclin A was not a prognostic factor. When subdividing according to ER status, cyclin A was a prognostic factor in the ER positive subgroup, but not in the ER negative (HR: 5.8, 95% CI: 2.2−16, $p < 0.001$) *vs*. 1.5 (95% CI: 0.6−3.9, $p = 0.44$). In multivariate analysis, cyclin A was an independent prognostic factor for DDFS (HR: 2.9, 95% CI: 1.2−7.0, $p = 0.018$), together with HER2 and age. Due to colinearity, histological grade and Ki67 were not included in the same model.

Conclusion: In this study cyclin A was an independent prognostic factor for premenopausal patients with node-negative breast cancer, but only in the ER positive subgroup. Similar to gene expression analyses, cyclin A can subdivide histological grade 2 breast cancer into two groups with different prognosis. Taken together, cyclin A may be an alternative or a complement to histological grade and Ki67 for prognostic considerations.

128 Poster

Locoregional recurrences in triple-negative, node-negative early stage breast cancer treated with breast-conserving treatment

T. Hijal[1], N. Gault[2], X. Sastre[3], A. Savignoni[2], M.A. Bollet[1], F. Reyal[4], A. Fourquet[1]. *[1]Institut Curie, Dept. of Radiation Oncology, Paris, France; [2]Institut Curie, Dept. of Biostatistics, Paris, France; [3]Institut Curie, Dept. of Pathology, Paris, France; [4]Institut Curie, Dept. of Surgery, Paris, France*

Background: Breast conserving-surgery followed by whole breast radiotherapy is standard of care in patients (pts.) with early-stage breast cancer. It is unclear if loco-regional control after breast-conserving therapy is affected by the tumor's phenotype. The aim of this study was to assess whether triple negative phenotype (TN: ER-ve and PR-ve and Her2-ve) was associated with locoregional recurrences (LRR) in node-negative patients.

Materials and Methods: We studied a consecutive series of 754 patients with node-negative breast cancer treated with breast-conserving treatment at the Institut Curie between 1995 and 1998. All pts. underwent breast-conserving surgery and axillary lymph node dissection, followed by whole breast irradiation. 22% of patients received a tumor bed boost while 50% received regional lymph node irradiation. Adjuvant systemic treatment was delivered to 18%. ER and PR status were determined by immunohistochemistry (IHC). HER2/neu status was determined by IHC, and confirmed by FISH in uncertain cases. Cumulative locoregional recurrence and survival rates of TN tumors were compared to other tumors using a log-rank test. Multivariate Cox proportional hazard model was used to determine independent predictors of loco-regional recurrence.

Results: Among the 754 pts., 81 (10.7%) were TN. Compared to other tumors, TN phenotype was more likely associated with non-ductal/non-lobular subtypes, and less often with lobular cancers; it was significantly associated with pT2 tumors, grade III, lympho-vascular invasion, and high mitotic index. With a median follow-up of 11.7 years, the 10-year cumulative rates of LRR were 19.2% in TN tumors and 13.9% in other tumors, ($p = 0.11$). TN tumors tended to occur earlier than other tumors. On multivariate analysis, only age and grade were significant, independent predictors of LRR. Ten-year survival rates were 70.5% in TN tumors and 88.7% in others, respectively ($p < 0.0001$).

Conclusion: This retrospective study with long follow-up confirms that, in pts. with node-negative breast cancer of whom only 18% had receivd adjuvant systemic treatment, TN phenotype was associated with a worse survival than other tumors. However, this study did not find a significant increase in loccoregional recurrences in TN tumors, whereas age and grade were significant predictors of LRR. It suggests that breast-conserving treatment can be carried out in pts. with TN tumors.

129 Poster

Down regulation of Heat Shock Protein 70 (HSP70) predicts responsiveness to neoadjuvant aromatase inhibitors in post-menopausal hormonal receptors expressing breast cancer

C.C.P. Yiu[1], H. Sasano[1], N. Chanplakorn[1], M.S.M. Chan[2], L.W.C. Chow[3]. *[1]Tohoku University School of Medicine, Pathology, Miyagi Prefecture, Japan; [2]UNIMED Medical Institute, Comprehensive Centre for Breast Diseases, Hong Kong, Hong Kong; [3]The University of Hong Kong, Li Ka Shing Faculty of Medicine, Hong Kong, Hong Kong*

Introduction: Aromatase inhibitor is an effective endocrine therapy in breast cancer patients expressing endocrine receptors. Our group has demonstrated changes in protein expression profile using proteomic approach before, ten proteins were found to have potential impact as predictors for AI responsiveness or resistance. In the present study, we test the change in expression profile of heat shock protein70 (HSP70), carbonic anhydrase 1 (CA1) and GDI in larger cohort of patients using immunohistochemical (IHC) staining.

Methods: Eligible post-menopausal breast cancer patients were recruited. Pre- and post-treatment tumour tissues were obtained and IHC staining was performed for targeted proteins. The changes of expression profile were compared to clinical response to determine the correlations.

Results: Total 32 patients, with both pre- and post-treatment carcinoma samples available, were recruited. Majority of patients responded to treatment (16 patients with PR, 14 with SD and 2 with PD). Increment in tumour size was observed in 4 patients (2 PD and 2 SD patients). Down-regulation of HSP70 was significantly associated with clinical responsiveness of AI treatment, $p = 0.014$; and change of proliferative index, Ki67, $p = 0.042$. Patients with pre-treatment high HSP level and proliferative index using Ki67 assay, were associated significantly with downregulation of HSP after treatment.

Conclusions: With the use of AI as neoadjuvant treatment, downregulation of HSP is associated with observed clinical response. Pre-treatment high HSP and Ki67 levels predict treatment response via their significant correlation with HSP downregulation. Therefore, pre-treatment HSP and Ki67 can be potential surrogate markers for AI treatment.

130 Poster

Small breast tumours with adverse prognosis

M. Sundquist[1], G. Tejler[2], L. Gustavsson-Wallander[1], S. Thorstensson[3], L. Brudin[4]. *[1]County Hospital, Surgery, Kalmar, Sweden; [2]Hospital, Surgery, Västervik, Sweden; [3]County Hospital, Pathology, Kalmar, Sweden; [4]County Hospital, Physiology, Kalmar, Sweden*

Background: Tumours less than 10 millimetres are often node negative, of grade 1 and have an excellent prognosis. However, even a tumour of a few millimetres would sometimes be mortal. We wanted to assess risk factors for dissemination of very small breast cancers.

Materials and Methods: The patient registry and pathology database were used to identify all patients with breast tumours less than 10 millimetres that were diagnosed 1985 to 2008 in the Kalmar county and their outcome. Multivariate analyses were carried out.

Results: 220 pts with tumours less than 10 mm were identified. 118 were grade 1, 73 grade 2 and 32 grade 3. HER2 was amplified and/or IHC 3+ in 36 cases. One or more lymph nodes were positive in 10 pts. Lymphovascular invasion (LVI) occurred in 13 cases. DCIS grade 3 of an extension of 15 mm or more accompanied 65 of the tumours.

During a median observation period of 9 years 20 pts, 9%, had distant metastasis. In the multivariate analysis HER2 positivity and the coexistence of extensive DCIS grade 3 were the only significant parametres, $p < 0.001$ and <0.006 resp.

Conclusion: Tumours less than 10 millimetres with extensive DCIS grade 3 and HER2 positivity have an increased risk of dissemination.

131 Poster

A straightforward but not piecewise relationship between age and lymph node status in Chinese breast cancer patients

K.D. Yu[1], Z.M. Shao[1]. *[1]Cancer Hospital, Breast Surgery, Shanghai, China*

Purpose: To investigate the relationship between age and axillary lymph node (LN) involvement in Chinese breast cancer patients, and to replicate a recently identified piecewise relationship between age and LN involvement.

Patients and Methods: A dataset, consisting of 3,715 patients (with complete information on study variables) with operable breast cancer consecutively surgically treated between 1996 and 2006, was derived from the database of Shanghai Cancer Hospital. Univariate and multivariate logistic regression were employed to analyze the relationship between age and LN. We subsequently performed a similar analysis on another dataset

including 1,832 consecutive patients treated between 2007 and 2008 to replicate our findings in the first dataset.

Results: A U-shaped relationship (previously observed in two European populations) between age and LN status failed to be replicated in our dataset of Chinese patients. Instead, we observed a linear rather than piecewise relationship. Moreover, the interaction between age and LN involvement was not modified by tumor size. After multivariate adjustment, the linear relationship was still present. The odds of LN involvement decreased by 1.5% for each year increase in age (OR 0.985, 95% CI 0.979–0.991, P < 0.001). Breast cancer subtypes were also associated with LN status. Proportions of basal-like and ERBB2+ subtypes decreased with increasing age. The observations in the first dataset were successfully replicated in a second independent dataset.

Conclusion: We confirmed a straightforward but not piecewise relationship between age and LN status in Chinese patients. The different pattern between Chinese and European elderly patients should be considered when making clinical decisions.

132 Poster

The change of tumour size between diagnosis and surgical treatment in breast cancer patients

J.W. Min[1], W.S. Han[1], H.G. Moon[2], J.H. Bae[1], S.K. Ahn[1], E.Y. Ko[1], J.H. Yu[1], I.A. Park[3], W.K. Moon[4], D.Y. Noh[1]. *[1]Seoul National University Hospital, Surgery, Seoul, South Korea; [2]Kyungsang National University Hospital, Surgery, Jinju, South Korea; [3]Seoul National University Hospital, Pathology, Seoul, South Korea; [4]Seoul National University Hospital, Diagnostic Radiology, Seoul, South Korea*

Background: Sometimes, patients who were diagnosed with breast cancer have to wait for surgery because of referral to and delay in tertiary care centers. These waiting time raise concerns for tumor progression. We evaluated the change in tumor size between diagnosis and surgical treatment by ultrasonography (US), and its correlation with upgrade of cancer stage, mastectomy rate, and prognosis. We also evaluated the clinical significance of tumor growth rate (TGR) determined by US in patients.

Materials and Methods: We identified 919 patients who were diagnosed invasive breast cancer from January 2002 to August 2009 in Seoul National University Hospital and who underwent US study at the time of first visit of our institute and at one day before surgery. We compared the change of ultrasonographic tumor size during these intervals. We excluded the patients who underwent neoadjuvant chemotherapy and had size difference of more than 1 cm between the final pathology and the last US before surgery. Disease free survival (DFS) was estimated using the Kaplan-Meier method.

Results: The median time duration from the first imaging study at our center to surgery was 27.5 days (range 8 to 92). The correlation coefficient between the last US and pathologic maximal tumor dimension was 0.906 (p < 0.0001). The median TGR (the change of tumor size in US/day) was 0.0083 cm/day. In a multivariate analysis, larger tumor size at the first imaging (p < 0.001), higher tumor grade (p = 0.01), ER negativity (p = 0.027), lymph node metastasis (p < 0.001), and perivascular invasion (p = 0.016) were significant predictors of higher TGR. There was a weak linear correlation between the time interval and change of tumor size (Pearson r = 0.114; p = 0.001). However, the time interval did not significantly affect the upgrade of T stage (p = 0.345) and mastectomy rate (p = 0.195). There was no difference in DFS between the patients with longer interval time (⩾28 days) and with shorter interval time (<28 days) (p = 0.918). Patients with higher TGR showed significantly worse DFS than patients with lower TGR (p = 0.039).

Conclusion: There was no evidence that longer interval time between diagnosis and surgical treatment leads to upstage, more mastectomy, or worse DFS. High tumor growth rate was a significant indicator for worse prognosis.

133 Poster

HER-2 and Ki-67 co-expression gives more prognostic information in breast cancer

T. Çolak[1], A. Mesci[1], E. Pestereli[2], S. Karaveli[2], M. Ozdogan[3], E. Alimoglu[4]. *[1]Akdeniz University, General Surgery, Antalya, Turkey; [2]Akdeniz University, Pathology, Antalya, Turkey; [3]Akdeniz University, Medical Oncology, Antalya, Turkey; [4]Akdeniz University, Radiology, Antalya, Turkey*

Introduction: HER-2 and Ki-67 have been extensively investigated on long term outcome of breast cancer. Immunohistochemical positivity of the HER-2 and Ki-67 in breast cancer cells were found associated with worse outcome in most of these studies. We investigated together effect of these markers on breast cancer outcome in this study.

Methods: A 10-year retrospective review was performed using the Breast Cancer Registry data at Akdeniz University Hospital, a tertiary care facility in Antalya, Turkey. A total of 736 patients with invasive breast cancer that underwent surgery between January 1999 and January 2009 were enrolled. The expression of HER-2 and Ki-67 in the tumor was assayed by immunohistochemistry in 406 patients. We accepted cutoff value for Ki-67 >15% and for HER-2 >30%++. Disease free survival (DFS) and overall survival (OS) were analyzed for the relation between conventional prognostic factors, HER-2, Ki-67, HER-2 and Ki-67 co-expression and clinical outcome. Patients follow-up time was median 58 months (range 4 to 128 months). A statistical analysis was performed by log rank test for univariate analysis and cox regression for multivariate analysis with SPSS 13.0 program and p < 0.05 was accepted significant.

Results: There were 65 (16%) distant recurrences and 50 (12%) death due to cancer in study period. Tumor size T status (P < 0.001, P < 0.001), axillary lymph node metastasis (P < 0.001, P < 0.001), axillary node status (P < 0.001, P < 0.001), pathologic stage (P < 0.001, P < 0.001), nuclear grade (P < 0.001, P < 0.001), histological grade (P = 0.001, P < 0.001), estrogen receptor status (P = 0.007, P < 0.001), HER-2 expression (P < 0.001, P < 0.001), Ki-67 expression (P = 0.015, P = 0.036), HER-2 and Ki-67 co-expression (P < 0.001, P = 0.001) were found influence of the DFS and OS by univariate analysis. Tumor size T status (P = 0.035, P < 0.001), axillary node status (P < 0.001, P < 0.001) and HER-2 and Ki-67 co-expression (P < 0.001, P = 0.003) were found independent risk factors for distance recurrence and death due to cancer by cox regression analysis (P value for DFS and OS given respectively). Estrogen receptor status (P = 0.012) were found independent risk factors for death due to cancer and axillary lymph node metastasis (P = 0.005), pathologic stage (P = 0.001), nuclear grade (P = 0.035) were found independent risk factors for distance recurrence. Five years DFS and OS were found 93%, 97% and 69%, 74% for two markers negative and two markers positive patient respectively (Table).

Conclusion: In addition to other conventional pathological factors, tumor growth and proliferation markers, such as HER-2 and Ki-67 predict outcome breast cancer patients. If these two markers are evaluated together, co-expression of both markers influences DFS and OS independent of conventional factors. In conclusion, if HER-2 and Ki-67 expressions assessed together may be gives more prognostic information in breast cancer.

HER-2	Ki-67	DFS (%±Std. Error)	OS (%±Std. Error)
negative	negative	93±3	97±2
negative	positive	88±3	92±3
positive	negative	82±5	88±4
positive	positive	69±5	74±5

134 Poster

Accumulation of p53 determined by immunohistochemistry as a prognostic marker in node negative breast cancer; analysis according to St Gallen consensus and intrinsic subtypes

S. Jung[1], H. Shin[2], S. Min[1], Y. Kwon[1], K.H. Shin[1], S. Lee[1], S.W. Kim[1], H. Kang[1]. *[1]National Cancer Center, Center for Breast Cancer, Goyang-si Gyeonggi-do, Korea; [2]Kwandong University School of Medicine, Department of Surgery, Goyang-si Gyeonggi-do, Korea*

Background: The purpose of the current study was to evaluate the prognostic impact of p53 accumulation by immunohistochemistry (IHC) in node-negative breast cancer and to determine the usefulness of p53 expression in subgroups according to St Gallen consensus and intrinsic subtypes.

Methods: A total 845 consecutive patients with LNN-BC that underwent surgery at the National Cancer Center, Korea between 2001 and 2005 were enrolled. We retrospectively reviewed the clinicopathologic characteristics and disease recurrence. The expression of p53 was assayed using immunohistochemistry (cut-off value: 10%, median value).

Results: The median age was 48 years (range: 25−85) and median follow-up period was 66.0 months (range: 9–101). Univariate analysis determined that tumor size, estrogen !!!receptor (ER), progesterone receptor (PgR), p53 (cut-off value: 10%), and Ki-67 (cut-off value: 15%) were significant for disease free survival (DFS). Of these factors, PgR negativity (HR 3.57, 95% CI 1.26–10.09, P = 0.01) and p53 positivity (HR 3.17, 95% CI 1.51–6.65, P =0.002) were identified as independent prognostic factors for DFS based on multivariate analysis. After then, we divided total patients into 4 intrinsic subtypes by expression of ER, PgR and HER2 and two risk groups (low-, intermediate-risk) by St Gallen consensus, and compared the DFS according to p53 expression in each subgroup. In luminal A, triple-negative subtypes and intermediate risk group, there were significant differences in the DFS rates. (5-yr DFS rate, luminal A; 97.2% for p53(−) vs 93.8% for p53(+); P = 0.03, triple-negative subgroups; 94.1%