Together We Challenge,
Together We Win!

Global Breast Cancer Conference 2013

GBCC 2013

October 10 (Thu.) - 12 (Sat.), 2013
Sheraton Grande Walkerhill Seoul, Korea

www.gbcc.kr

ABSTRACT BOOK

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GBCC2013

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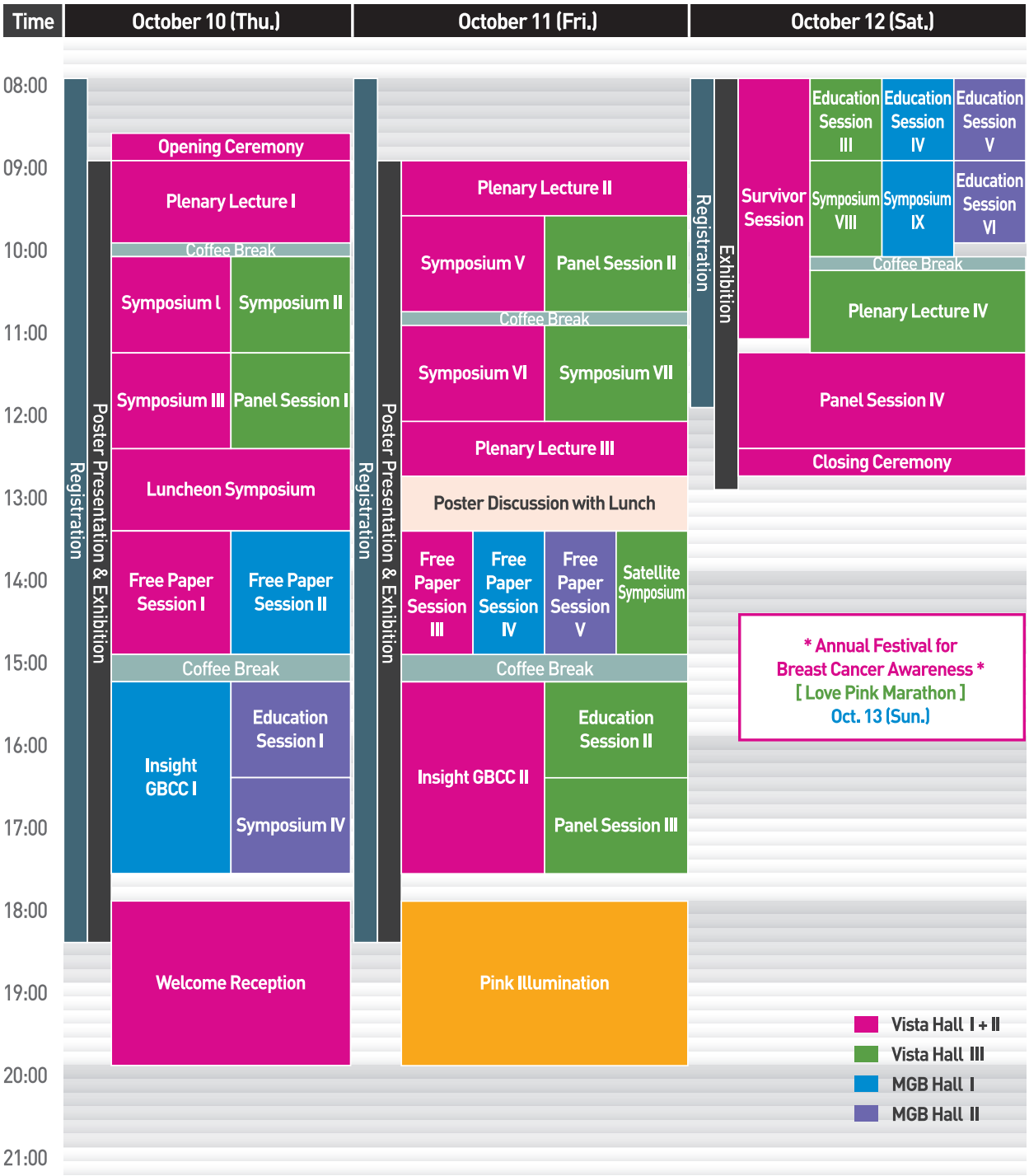
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Opening Ceremony

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October 12(Sat.), 2013

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[2] *Dept. of Surgery, Tungs' Taichung MetroHarbor Hospital, Taiwan*
[3] *Dept. of Life Science, National Chung Hsing Univ., Taiwan*
[4] *Graduate Institute of Cancer Biology, China Medical Univ., Taiwan*
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[1] *Dept. of Breast & Endocrine Surgery, Kumamoto City Hospital, Japan*
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[1] *Dept. of Surgery, Konyang Univ. Hospital, Korea*
[2] *Dept. of Surgery, Medical School, Chonbuk National Univ., Korea*
[3] *Dept. of Surgery, Chonnam National Univ. Hwasun Hospital, Korea*
[4] *Dept. of Surgery, College of Medicine, Chungnam National Univ., Korea*
[5] *Dept. of Surgery, College of Medicine, Dankook Univ., Korea*
[6] *Dept. of Surgery, Soonchunhyang Univ. Hospital, Korea*
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[1] *Divison of Breast and Endocrine Surgery, Dept. of Surgery, College of Medicine, Korea Univ. Hospital, Korea*
[2] *Divison of Breast and Endocrine Surgery, Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

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[1] *Dept. of Surgery, Univ. of Ulsan, ASAN Medical Center, Korea*
[2] *Dept. of Oncology, Univ. of Ulsan, ASAN Medical Center, Korea*
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[1] *Dept. of Pathology, Assam Medical College, India*
[2] *Dept. of Surgery, Assam Medical College, India*

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GBCC2013

Plenary Lecture

PL01

PERSONALIZED THERAPY IN ERA OF MOLECULAR DIAGNOSIS

Nancy E. Davidson

Cancer Institute, Univ. of Pittsburgh Cancer Institute, U.S.A.

Today breast cancer is recognized as a family of diseases with distinct molecular features that provide the opportunity for more precise therapy. Through rigorous clinical investigation and an improved understanding of the systemic nature of the illness many patients can now be successfully treated with lumpectomy, sentinel node localization, and accelerated radiation. Molecular subtyping has identified at least four major types of breast cancer.

Luminal A breast cancers are highly response to endocrine therapy. The availability of anti-HER-2 therapy has changed the natural history of HER-positive disease. Substantial challenges remain in the management of luminal B disease where endocrine therapy does not appear to be sufficient for many patients and in “triple negative” disease where cytotoxic therapy is the treatment of choice in the absence of specific targeted agents. Skillful use of these approaches can lead to good long term outcomes for many women though much remains to be accomplished, especially for those women who develop metastatic disease, an area of great unmet need. Findings from the large genomic characterizations of primary breast cancers have confirmed the multiplicity and diversity of genomic changes within each breast cancer and provide the challenge of how to harness this information clinically. This will require careful attention to testing and the development of new trial designs to establish the use of these next generation sequencing approaches to select therapy.

Finally, it is clear that breast cancer is in part a preventable disease. Evidence-based approaches to genetic testing for BRCA1/2, use of tamoxifen or raloxifene for high risk women, and an emphasis on maintenance of appropriate BMI should help to reduce the diagnosis of breast cancer while age-appropriate screening should aid in early detection. This multi-pronged approach should help to decrease the global burden of breast cancer.

PL02

NEOADJUVANT THERAPY FOR BREAST CANCER

Soonmyung Paik

Division of Pathology, National Surgical Adjuvant Breast and Bowel Project(NSABP) Foundation, Inc., U.S.A.

Current system of regulatory approval based on survival end point is too lengthy and resource hungry. Surrogate marker based trial mechanism is an attractive alternative if a valid surrogate for survival outcome can be found.

While complete pathological response (pCR) was hypothesized to be that surrogate endpoint. However results from NSABP trial B-27 trial rejected the hypothesis.

FDA has organized a global collaboration among clinical trial groups that have conducted randomized trials in neoadjivant setting called CTNeo Meta-Analysis.

Four questions were addressed; (1) Is pCR associated with long term outcomes (EFS and OS)? (2) Which pCR definition associates better with long term outcome? (3) In which breast cancer subtypes pCR associates with long term outcome? (4) What pCR delta will predict long term clinical benefit (EFS and OS improvement)?

Individual level data from 11,955 patients enrolled in 12 randomized clinical trials were analyzed and reported at the 2012 San Antonio Breast Cancer Symposium by Dr. Patricia Cortazar from FDA.

In this talk, I will review her presentation and discuss challenges in accepting pCR as surrogate endpoint for drug approval process and discuss concepts of post-neoadjuvant trial as a potential solution to the regulatory challenges.

PL03

TAILORED ADJUVANT THERAPY BASED ON GENOMIC ASSAYS

Hope S. Rugo

Dept. of Medicine, Univ. of California San Francisco Medical Center, U.S.A.

The goal of treatment for early stage breast cancer is primarily to prevent distant recurrence. Adjuvant and neoadjuvant therapy is given to eliminate occult or microscopic metastatic cells, and can include multiple modalities. Until relatively recently, treatment was based on extent of disease and patient age, dividing women with breast cancer into pre- or post-menopausal by age, and node positive or not, then using these two parameters to decide on the type and extent of systemic therapy. Current standards require that treatment be adapted to a better understanding of tumor subtypes, starting with the presence or absence of gene amplification or protein expression of HER2/*neu*, and expression of hormone receptors. Patients with HER2/*neu* positive disease almost always receive treatment targeted to HER2 in combination with chemotherapy, and outcome in that setting has been very good. Despite several studies evaluating molecular markers to predict benefit from HER2 targeted therapy, the best predictor of response remains HER2 gene amplification or protein expression. Similarly, patients with cancers that do not express either HER2/*neu* or hormone receptors are almost always treated with chemotherapy as to date, no other effective systemic treatment options exist. There appears to be marked heterogeneity among triple negative cancers, although we do not understand how to apply this heterogenity to clinical decisions

Patients with hormone receptor positive tumors have a number of choices for optimal adjuvant treatment. Certainly for the majority, hormone therapy is a critical component of this prescription, with recent data supporting longer duration of therapy. However, the use of chemotherapy has been controversial. In what tumors, what patients? We learned from the neoadjuvant setting that a minority of patients with hormone receptor positive disease achieve a pathologic complete remission following neoadjuvant chemotherapy, yet these patients often have an excellent prognosis. This would suggest that at least a subset of these tumors could do well without adjuvant chemotherapy. Although clearly size and extent of disease are important, an understanding of tumor biology will give us the best insight into appropriate use of chemotherapy in this disease.

Two genomic tests, the Recurrence Score and Mammaprint, have demonstrated that gene expression of a panel of genes has the ability to provide prognostic information for early stage breast cancer. Using archived tumor samples from two NSABP trials, the Recurrence Score also was able to predict benefit from chemotherapy in patients with hormone receptor positive and node negative breast cancer. The addition of clinical and pathologic factors has allowed further delineation of prognosis. Subsequent studies have not allowed differentiation between different types of chemotherapy, or different types of hormone therapy. However, it is clear that the biology of an individual tumor is a critical factor in tailoring the type of adjuvant therapy that is most likely to reduce the risk of recurrence. In prospective studies evaluating the impact of the Recurrence Score on treatment decisions, the largest percentage of patients are those that would have received chemotherapy before knowing the results of the test, but now are treated with hormone therapy alone, sparing the toxicity of chemotherapy.

However, a significant number of patients would not have received chemotherapy before the results were available, putting them at higher risk of recurrence.

Future studies are hoping to define tumors with a higher risk of late versus early recurrence, and two large completed phase III trials incorporated the Recurrence Score and Mammaprint respectively in the determination of appropriate adjuvant therapy which we will discuss in detail. An ongoing study, TailoRx, is evaluating use of the Recurrence Score in node positive, hormone receptor positive disease. The current available genomic tests provide important information that has a significant impact on treatment decisions for women with early stage breast cancer. Our goal moving forward is to further improve and define tests that will allow us to choose the most effective therapy for an individual tumor.

PL04

STRESS AND BREAST CANCER: THE EFFECTS OF STRESS MANAGEMENT INTERVENTION ON BIOBEHAVIORAL PROCESSES

Michael H. Antoni

Dept. of Psychology, Univ. of Miami, U.S.A.

The stressors associated with diagnosis and primary treatment for breast cancer are numerous and can affect multiple aspects of quality of life and health outcomes. Patients undergoing breast cancer (BCa) diagnosis, surgery and adjuvant therapy reveal differences in psychological adaptation that are predicted by cognitive (stressor appraisals), behavioral (coping strategies) and interpersonal (social support and interpersonal skills) factors on the one hand and related to alterations in health-relevant neuroendocrine and immunologic indicators on the other. Through longitudinal observational studies we initially identified cognitive, behavioral and interpersonal predictors of psychological adaptation to the stress of BCa treatment. Using genome-wide transcriptional profiling and bioinformatics analyses, we observed that indicators of poorer adaptation in the period after surgery were associated with more inflammatory signaling (cytokines, and chemokines) in circulating leukocytes. This may be particularly relevant in the context of cancer treatment, since inflammation may relate to greater symptomology, delayed recovery and disease progression.

Since poorer psychological adaptation is associated with pro-inflammatory transcriptional profiles in circulating leukocytes in women undergoing primary treatment for BCa, it follows that psychosocial interventions that improve adaptation (through cognitive, behavioral and interpersonal skills training) may alter neuroendocrine and leukocyte functioning. We tailored a group-based cognitive behavioral stress management (CBSM) intervention to modify these processes during primary treatment for non-metastatic BCa. The CBSM intervention was a 10-session weekly group where women learned relaxation methods (muscle relaxation, imagery, breathing), cognitive/behavioral techniques (cognitive restructuring and coping effectiveness training) and interpersonal skills (anger management and assertiveness training).

We tested the effects of the CBSM intervention against an active psychoeducation control condition in a series of randomized controlled trials. The aims of the trials we conducted with CBSM were to: (a) improve psychological adaptation as women moved through treatment, and (b) examine whether these changes were paralleled by neuroendocrine and immune/inflammatory changes that could have health implications. Women were recruited in the first 2 months after surgery (before initiating adjuvant treatment) and completed questionnaires and blood draws at baseline (pre-randomization) and at 6 and 12-month follow-up. Over a 12-month observation period, women assigned to CBSM showed increased positive affect, and decreased negative affect (and improved on several other psychological adaptation indicators) whereas controls showed negligible change over time. Over this period women in CBSM also revealed decreases in PM serum cortisol levels and increases in Th1 cytokines by stimulated leukocytes. Leukocyte gene expression studies indicated that 62 transcripts showed significantly greater than 50% down-regulation of genes associated with inflammation over time in CBSM-treated patients relative to controls, including genes encoding pro-inflammatory cytokines, COX2, and inflame

matory chemokines and their receptors. We also found greater down-regulation of genes associated with cancer promotion in CBSM vs. controls including those involved in tissue remodeling and epithelial-mesenchymal transition (e.g., MMP9). Approximately 50% of the genes showing down-regulation during CBSM were those shown to be associated previously with poor psychological adaptation. By the 12-month follow-up women assigned to CBSM continued to show only about half the gene expression for many inflammation genes and cancer promotion genes compared to controls. Gene Ontology analyses confirmed that CBSM down-regulated genes were characterized by involvement in pro-inflammatory cytokine activity and wound healing. We also found that women in CBSM revealed increased leukocyte gene expression for Type I Interferon signaling. Promoter-based bioinformatics analyses implicated decreased activity of NF-κB/Rel and GATA family transcription factors and increased glucocorticoid receptor activity in myeloid cells as potential mediators of CBSM-induced transcriptional alterations.

This talk will describe the nature of CBSM intervention, and summarize its effects on positive and negative indicators of psychological adaptation, and neuroendocrine and immunologic parameters. Evidence is presented for putative mediators of intervention effects on psychological adaptation, and for leukocyte cell-signaling changes that might begin to explain intervention effects on biological processes involved in cellular immune function and inflammation. Ongoing studies following these women over a longer-term basis for effects on adaptation and clinical disease endpoints are noted. Ongoing dismantling research is described as one approach to elucidate key intervention components (e.g., relaxation skill vs. cognitive-behavioral skills) that could account for observed effects in this population. With the multiple stressors associated with BCa diagnosis and treatment, and evidence that stress can affect health-relevant neuroendocrine and immunologic processes, it is plausible that offering stress management interventions that facilitate psychological adaptation during primary treatment for cancer may be used as a supportive procedure. These interventions show evidence for modulating biobehavioral processes that could have implications for recovery after adjuvant therapy, and possibly longer-term quality of life and health outcomes in breast cancer survivors. Since emerging work shows that these forms of psychosocial intervention may increase survival and reduce disease recurrence in breast cancer patients, our work provides insights into how these interventions impact biobehavioral processes during the first year of treatment, which may influence the health trajectory into the survivorship period.

GBCC2013

Symposium

SY01-1

RECURRENCE PREDICTIVE MARKERS FOR DCIS

Gary Tse

Dept. of Anatomical and Cellular Pathology, Prince of Wales Hospital, Hong Kong

Ductal carcinoma *in situ* (DCIS) represents neoplastic proliferation of malignant cells confined to ductal lobular units. It constitutes 15-30% of all newly diagnosed breast cancers, and has an inherent tendency to progress to invasive disease. As DCIS is pre-invasive and does not usually metastasize, the breast cancer specific mortality is low, and is reported to be 1-2.6% 8-10 years after diagnosis. DCIS is a heterogeneous disease, and basing on the molecular progression pathway, it can be grouped into low grade and high grade diseases with different molecular signatures and marker profiles. The intermediate grade category appears to lack distinctive signature and probably represents a mixture of high grade and low grade cases. In the treatment of DCIS, local excision remains the mainstay treatment, and addition of radiotherapy is associated with significant reduction of rate of recurrence. Nevertheless, the impact on patients' overall survival is much less.

To predict recurrences of DCIS, many factors and biomarkers have been evaluated. These can be divided into traditional predictors and biomarkers.

Traditional predicts are factors based on patient and tumor characteristics. Patients factors include younger age and symptomatic (Mammographic detection, mass formation) DCIS. Tumor factors include different architectural, with cribriform, papillary, solid and mirocpapillary types DCIS showing lower recurrence rate than comedo architecture. Nuclear grade is an important and high to very high nuclear grade are associated with higher recurrence rate. Comedo necrosis is also a recurrence predictor, but appears to be weaker than nuclear grade or architectural type. These three factors (i.e. architecture, comedo necrosis and nuclear grade are all interrelated and are frequently associated with each other). Other tumor factors such as larger size and closer to margin at excision are also proven predictors for recurrence. The Van Nuys Prognostic index incorporates all these factors (size, margin, necrosis, nuclear grade and patient age) to give a score that has a guidance effect for treatment of patients.
Specific predictors for invasive recurrences (which are more serious and potentially leading to mortality) are less well defined.

Similar to invasive breast cancers, DCIS can also be grouped into similar molecular subtypes, and it was found that luminal A cancers show a lower recurrence risk than luminal B cancers, and HER2 group of cancers show increased recurrence risk. Biomarkers that were found to be most useful were HER2, ER and markers related to Rb pathway. These may be potential therapeutic targets. Recently a multigene assay has been evaluated using a panel of 12 genes including proliferation group, hormone receptor group and GSTM1, and resulting DCIS score quantifies local recurrence risk.

SY01-2

IMAGING CONTROVERSY IN DCIS SURVEILLANCE

Hee Jung Shin

Dept. of Radiology, ASAN Medical Center, Korea

DCIS is a breast malignancy that is characterized by the proliferation of malignant ductal epithelial cells without evidence of invasion through the basement membrane. Coincident with the increased use of mammography has been a marked increase in the detection of DCIS. Before the era of mammographic screening, DCIS represented less than 5% of all malignancies of the breast. DCIS now accounts for between 20% and 40% of all nonpalpable cancers detected at screening and about 20% of all newly diagnosed cancers. All cases of invasive ductal carcinoma are believed to develop from DCIS, but not all cases of DCIS progress to invasive ductal carcinoma. Critics of screening have referred to DCIS as a pseudocancer, false positive, and harm from screening which leads to unnecessary biopsies and excessive surgery. Justification for the use of DCIS as an index of the benefit of screening depends on how often and how rapidly DCIS evolves into invasive ductal carcinoma. No direct method exists for determining the natural progression of DCIS. If patients with DCIS were never to undergo biopsy and the DCIS were left to develop into invasive carcinoma, there would be no way to establish that the initial lesion was DCIS. If DCIS is completely excised, its natural history has been stopped, but there is no proof that it would have evolved into invasive ductal carcinoma.
Results from autopsy studies of women with no clinical evidence of breast cancer show a 6% to 14% prevalence of DCIS. These rates have been used to suggest that most cases of DCIS may never become clinically apparent. However, there are reasons why this conclusion is not justified. Firstly, most of the autopsy-detected cases could not be identified by radiography performed on the surgical specimens. Secondly, detection rates for invasive ductal carcinoma at prevalence screening are two to three times higher than the expected incidence. Moreover, some cases classified as DCIS in the autopsy studies, which took place in the 1980s, would be reclassified as atypical hyperplasia according to current histology criteria. Based on a statistical model using the numbers of DCIS and invasive cancers detected at five different screening programs, Yen and colleagues estimated that among cases of DCIS dectected at initial screening, 63% were progressive and 37% were nonprogressive. At incidence screenings, 96% of detected cases of DCIS were progressive and only 4 % were nonprogressive.

Mammography is the primary tool for detecting DCIS, but it has limitations especially in women with dense breast tissue. The most common mammographic findings of DCIS is the presence of microcalcifications, but a low-grade lesion without necrosis is less likely to manifest as calcifications than either an intermediate- or a high-grade lesion. Other mammographic findings might include a mass or architectural distortion. Other findings, such as masses, architectural distortions, dilated retroareolar ducts, and developing densities, have also been reported. In one study involving a higher percentage of low-grade lesions, DCIS manifested as a mass in 40% of cases. Although most cases of DCIS are diagnosed mammographically, 6-23% of DCIS lesions are not visible on mammography.

Mammography plays a key role in the detection of DCIS, in which calcifications are the mammographic hallmark. The typical appearance is fine, linear, discontinuous, and branching calcifications with a diameter of usually less than 0.5 mm. Mammographically, microcalcifications of noncomedo DCIS are granular, hazy, amorphous, or indistinct particles characterized by variable size and shape. In contrast, the individual calcifications of comedo DCIS are likely to be larger and more coarse as well as discontinuous, linear, and branching. However, these radiographic features are not always reliable in differentiation among the histologic subtypes of lesions. Several studies have examined the role of US in the evaluation of DCIS. One study showed that imaging finding of noncalcified DCIS were nonspecific, often appearing similar to those of invasive masses. In addition, MRI has higher sensitivity thant mammography for the detection of DCIS and greater accuracy for depicting the extent of disease. Kuhl et al. reported that 92% of DCIS were diagnosed by MRI and 56% by mammography and other previous study showed that the sensitivity of MRI was 94% and that of mammography was 86% for the detection of DCIS.

In this lecture, I would like to show the various imaging features of DCIS and differential diagnosis of DCIS. In addition, I'd like to present how we precisely determine the extent of calcified and noncalcified DCIS and how we search the coincident and subsequent malignancy.

SY01-3

SCANXIETY: CONTROLING FEAR OF CANCER

Juhee Cho

Cancer Education Center, Samsung Comprehensive Cancer Center, Korea

SY02-1

BREAST CANCER EPIDEMIOLOGY AMONG ASIANS : HETEROGENEITY BY COUNTRY, AGE GROUPS AND RACE/ETHNICITY

Yeonju Kim

Dept. of Epidemiology Program, Univ. of Hawai'i Cancer Center, Korea

Breast cancer incidence and mortality rate and their secular trends have been suggested to differ between countries, age groups, and race/ethnicity. The aim of this presentation is to review the rates and the trends of incidence and mortality of breast cancer focusing on Asian women.

Geographic Comparison of Breast Cancer Incidence Rate

Breast cancer is the most common cancer in women worldwide of 1.38 million incident cases in 2008 [1]. The estimated age-standardized incidence rate (ASIR) per 100,000 of breast cancer in Asian countries ranges from 24.0 in south-central Asia to 32.5 in Western Asia, which are lower than the worldwide average of 39.0.

The ASIR of breast cancer among Asian women varies in Asian countries. Among 49 Asian countries in GLOBOCAN 2008, the eleven countries with the highest ASIR of breast cancer per 100,000 are Israel (96.77), Singapore (59.87), Lebanon (55.38), Taiwan (52.75), Bahrain (49.79), Kuwait (47.73), Armenia (47.26), Jordan (47.01), Maldives (46.03), Japan (42.7), and South Korea (38.89). China ranked as the 36th (ASIR 21.64), and countries with the lowest ASIRs were Bhutan and Mongolia of ASIR 8.00. Breast cancer incidence rate also varies within different regions of the same country. The ASIRs of breast cancer in China are 19.2 in rural regions, 52.2 in Shanghai, and 65.2 in Hong Kong [2].

Breast cancer incidence rates in Asia are increasing rapidly in eastern Asia, south Asia, and southeast Asia, while those slightly increased in North America and western Europe[3].

Breast Cancer Incidence Rate by Age Groups and Race/Ethnicity

The breast cancer incidence rate among women in the United States is different by race/ethnicity and age groups. Among non-Hispanic white women, it was increased from 1975 to 1999, decreased from 1999 to 2005, and slightly increased in the recent years from 2005 to 2009[4]. In contrast, breast cancer incidence rate among the Asian population increased steadily in the United States. In the Los Angeles Cancer Surveillance Program from 1972 to 2007, breast cancer incidence rates among several Asian racial/ethnic groups (Japanese, Chinese, Filipino, and Korean) increased steeply. Chinese and Korean women who had shown the lowest breast cancer rate were replaced with Hispanic women[5]. In a recent analysis using the Surveillance Epidemiology and End Results (SEER) data collected from Hawai'i between 1975 and 2005, breast cancer incidence rate decreased among white women of age 65+ and increased among white women of age groups of 20-49 and 50-64. However, among Asian racial/ethnic groups including Japanese, Filipino, and Chinese, breast cancer incidence rate increased in every age group (20-49, 50-64, and 65+). Particularly, among Japanese, stage I invasive breast cancer among women older than 50 years increased, while stage II and III cancers did not. Cross-over patterns of breast cancer incidence rates by race/ethnicity were examined in Asia. In Singapore breast cancer incidence rate among the Indians was higher followed by the Chinese and Malay

women until 1985; the rates among Chinese and Malay women rapidly increased, and since 1985, Chinese has shown the highest rate while Indian has shown the lowest rate [6] .

Breast Cancer Mortality Rate by Country and Race/Ethnicity

The estimated breast cancer deaths were 458,000 and age-standardized mortality rate was 12.5 worldwide in GLOBOCAN 2008. Mortality rates in Asian regions were 6.3 in eastern Asia, 12.0 in south-central Asia, 13.4 in south-eastern Asia, and 14.3 in western Asia. Rates and trends of breast cancer mortality in Asian countries are not unitary. During 1975-2006, breast cancer mortality rates steadily increased in Korea, Japan, and Taiwan, while the rates slightly decreased in Hong Kong and Singapore among women age 70+ from 1990[7.] In the United States, compared to non-Hispanic whites, the risks of breast cancer death were 20% higher among Filipino and 30% lower among Japanese, and no association was observed in other Asian subgroups [8]

Conclusions

Asians residing in Asia have relatively a low rate of breast cancer incidence, but the secular trend shows a rapid increase. A similar increasing trend was examined among Asians residing in Northern America. On the contrary, trends of breast cancer mortality rates varied in Asian countries and by racial/ethnic groups. It has been suggested that the increasing trend of breast cancer incidence rate is related to the rapid change of lifestyle, and the differences in mortality rate is determined by socioeconomic status and preventive strategies of breast cancer in each country.

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SY02-2

LIFESTYLE FACTORS AND BREAST CANCER (BC) RISK

Pamela Goodwin

Division of Medical Oncology and Hematology, Division of Clinical Epidemiology, Univ. of Toronto, Samuel Lunenfeld Research Institute at Mount Sinai Hospital, Canada

Obesity has been associated with an increased risk of postmenopausal BC [Relative Risk (RR) 1.12 per 5 kg/m2 increase in Body Mass Index (BMI), 95% Confidence Intervals (95% CI) 1.08-1.16], and a decreased risk of premenopausal BC (RR 0.92 per 5 kg/m2, 95% CI 0.88-0.97). A recent meta-analysis has reported an increased risk of estrogen/progesterone receptor (ER/PgR) positive BC of 33% (95% CI 20-48%) for each 5 kg/m2 increase in postmenopausal women but a decreased risk of 10% (95% CI 18-1% decrease) in premenopausal women; there was no association of BMI with risk of hormone receptor negative BC, regardless of menopausal status. Obesity is also associated with poor BC outcomes, regardless of menopausal or hormone receptor status. Adult weight gain has been associated with increased risk of ER/PgR positive BC, predominantly in postmenopausal women (RR 2.33, 95% CI 2.05-2.60). There is some evidence that BCs developing in obese women are larger with more frequent axillary node involvement. Higher birth weight has been associated with increased BC risk, notably of ER/PgR positive BC. A recent meta-analysis identified a RR of 1.07, 95% CI 1.02-1.12 per 1 kg increase in birth weight, with similar associations seen in early vs. late onset BC.

Higher lifetime physical activity has been associated with a modest reduction in BC risk in numerous studies. The Nurses' Health Study identified a RR of 0.82 (95% CI 0.70-0.97) in women who exercised 7 hours weekly vs. <1 hour weekly. Vigorous physical activity may lead to greater risk reduction. Associations of physical activity with BC risk may be strongest in postmenopausal women.
Dietary fat intake has been inconsistently associated with BC risk in observational studies. In the Women's Health Initiative (WHI) diet intervention trial, those randomized to a reduced fat diet (vs. usual diet) had a modest reduction in BC risk that was of borderline statistical significance ((HR 0.91, 95% CI 0.83-1.01, p=0.06).

Potential biologic mechanisms for these energy-balance related factors include elevation in estrogen levels, the development of insulin resistance (increased insulin, glucose, inflammatory markers couple with altered adipokines) or local effects in the breast (localized inflammation with associated increased in cytokines). Although higher estrogen levels in obese postmenopausal women are widely believed to mediate these obesity effects, a recent exploratory analysis conducted in the WHI Observational Study provided evidence that obesity associated hyperinsulinemia may play a greater role.
Alcohol intake has been associated with increased BC risk. Meta-analyses suggest that consumption of as little as 1 drink per day is associated with a RR of 1.04 (95% CI 1.01-1.07 while consumption of ≥3 drinks per day is associated with a HR of1.3 to 1.4. Overall, RR increases by about 10-13% for each 10 gram (about 1 drink) of alcohol consumption each day. These associations appear to be strongest for hormone receptor positive BC. The biologic basis for these associations may include elevations in estrogen and acetaldehyde levels, as well as genotoxic effects of alcohol.

Smoking has been associated with increased BC risk in recently conducted studies. Increased amount and duration of smoking increase BC risk by 15-40%; this association may be strongest in women with N-acetyltransferase2 gene slow acetylation genotypes. Second hand smoke exposure has also been associated with increased risk of premenopausal BC. Mammary carcinogens in tobacco smoke are believed to mediate this association.

In the face of a growing obesity epidemic, the impact of obesity on BC risk and outcomes at a population level is a major public health issue. Intentional weight loss through lifestyle change, as well as weight loss after bariatric surgery, have been associated with reduced BC risk and/or mortality. The observation that higher birth weight is associated with increased BC risk raises concerns about transgenerational transmission of risk. Research into clinical and public health interventions that counter obesity are strongly recommended as is research designed to enhance understanding of biologic mediators of the lifestyle-BC associations, with a potential goal being to develop targeted pharmacologic interventions. Observations that metformin may be associated with reduced BC risk and improved outcomes have led to interventions trials, primarily in the setting of established BC.

SY02-3

PUBLIC HEALTH SURVEILLANCE AND BREAST CANCER PREVENTION AGENDA

Insun Kim

National Center for Health Statistics, Centers for Disease Control and Prevention, U.S.A.

SY03-1

DISCREPANCIES BETWEEN IDEALS AND REALITY IN KOREA

Kyung Hae Jung

Dept. of Oncology, ASAN Medical Center; Univ. of Ulsan College of Medicine, Korea

Every patient has been provided with national health insurance in Korea since 1989 and patients with severe disease including cancer have made payment of only 5% of all medical cost if covered by insurance. However, limited resources are one of the main problems and restrict use of modern, especially expensive, medications. Followings are typical examples.

Patients with HER2-positive tumors have benefit from treatment with HER2 targeted agents in combination with cytotoxic drugs. Recently NCCN guideline recommends pertuzumab plus trastuzumab in combination with a taxane as a preferred option for the first-line treatment of patients with HER2-positive metastatic breast cancer (MBC). However, pertuzumab is not available now and outlook of its reimbursement in the near future is very dim in Korea. Several trials have showed benefit of continuation of trastuzumab therapy following disease progression on a trastuzumab-containing regimen in HER2-positive MBC. But continuation of trastuzumab with other cytotoxic drug has not been allowed unfortunately when progressed on first-line trastuzumab-containing regimen or prior exposure (within one year) to trastuzmab in adjuvant setting.

Incorporation of trastuzumab into chemotherapy regimens is accepted as standard treatment in HER2-positive tumors treated with neoadjuvant chemotherapy. Addition of trastuzumab to taxane ± anthracycline-containing regimen is associated with increase in pCR rate. Recent update of NOAH trial revealed pathologic complete remission (pCR) with trastuzumab is linked to significant event-free survival (EFS) benefit, while association with pCR and EFS is smaller and non-significant without trastuzumab. But the cost of neoadjuvant therapy is not reimbursed by insurance if used with trastuzumab and almost of all patients give up the benefit of pCR because of economic burden.
Moreover, taxane has not been approved yet in node-negative breast cancer. Thus patients with high risk node-negative breast cancer, such as triple negative cancer, should omit taxane in their adjuvant chemotherapy.

These discrepancies between ideals and current practices restricted by insurance and regulations are big obstacles for oncologists to overcome.

SY03-2

NEOADJUVANT THERAPY FOR EARLY BREAST CANCER IN HER2 TYPE AND LUMINAL TYPE TUMORS

Hirotaka Iwase

Dept. of Breast and Endocrine Surgery, Kumamoto Univ., Japan

To evaluate the clinical, pathological and biological responses of potential anti-tumor agents, neoadjuvant therapy is usually adopted for operable breast cancer according to tumor biology.

In Japan, Trastuzumab (Tmab) was approved in 2001 for metastatic HER2 positive breast cancer (mBC) without any limitation of treatment duration. In 2008, adjuvant therapy with Tmab was approved for early breast cancer (eBC), based on the results of HERA, NSABP B-31, and N9831. Since 2011 Tmab could be used as a neoadjuvant therapy for stage II/III HER2 positive eBC. In practice, an anthracycline-containing regimen followed by Tmab plus taxane shows the best pathological complete response (pCR) rate of over 50% of the treated patients. Although lapatinib was approved for HER2 positive mBC only in combination with capecitabine in 2009, the combination of lapatinib with Tmab has not yet been approved for use. This combination trial is currently in progress by the Japanese Breast Cancer Research Group with reference to neo-ALTTO and NSABP-B41.

Neoadjuvant endocrine therapy with an LHRH agonist plus tamoxifen can be adapted for premenopausal women with ER positive/HER2 negative operable breast cancer. To compare the efficacy and safety of goserelin plus tamoxifen with goserelin plus anastrozole in the neoadjuvant setting, we performed a phase 3, randomized, double blind, multi-center study. The response rate of goserelin + anastrozole was much higher than that of goserelin + tamoxifen (anastrozole 70.4% [69 of 98 patients] vs. tamoxifen 50.5% [50 of 99 patients]; estimated difference between groups 19.9%, 95% CI 6.5-33.3; p= 0.004). In Japan the combination of an LHRH agonist plus an aromatase inhibitor has, however, not been approved yet.

These are typical examples of the discrepancies between insurance based on clinical practice and the most up-to-date scientific knowledge.

SY03-3

CHALLENGES OF THE "SECOND WAVE" OF PERSONALIZED MEDICINE – THE HONG KONG BEDSIDE EXPERIENCE

Janice Tsang

Dept. of Clinical Oncology, Queen Mary Hospital; The Univ. of Hong Kong, Hong Kong

Thanks to our better understanding of tumour biology and the development of various anti-cancer and targeted agents, breast cancer has been known to be heterogeneous disease. Since the identification of the HER-2 receptor and the advent of anti-HER2 therapy coming into place in the 2000s, there have been further new developments bringing personalized management for breast cancer patients a reality. These include the emerging and exhausting list of targeted agents such as various anti-HER2 agents, the mTOR inhibitors, new chemotherapeutic agents, leading to proposal of different combination of treatment options dedicated for selected groups of patients. Furthermore, the recent advances in molecular genomic profiling has further led us to a "second wave" of personalized medicine – predicting the benefits of a particular treatment for a particular patient, or trying to spare some patients from any unnecessary toxicities such as chemotherapy.

However, the clinical decision making for our breast cancer patients is always a complex process. The breast cancer outcome is a function not only of innate biological factors, but also of modifiable characteristics of individual behaviour, patient and family decision making values, the unique cultural, psychosocial factors, the characteristics of healthcare system relevant to a particular country or region, as well as the challenge of matching science with affordability.

This sharing session will address some of the aforesaid challenges using real clinical examples based on the bedside experience in a tertiary institution of Hong Kong.

SY03-4

BREAST CANCER MANAGEMENT ISSUES IN THE CLINIC AS AN ONCOLOGIST? CASES FROM MALAYSIA

Cheng Har Yip

Breast Centre, Sime Darby Medical Centre, Subang Jaya, Malaysia

Malaysia is a multiethnic country with three main ethnic groups, that is, Malays, Chinese and Indians. Patients also come from different socio-cultural backgrounds and it is important to be culturally sensitive when counselling women presenting with breast symptoms. Communication can be a major problem when we have a patient who speaks a language that the doctor is unable to understand.
The majority of patients with a breast lump is referred to the surgeon, and since there are less than 25 breast surgeons in the country with a population of 26 million people, most breast cases are handled by the general surgeon.

The role of the surgeon is to diagnose breast cancer in a timely fashion, with triple assessment ie clinical assessment, imaging and a percutaneous biopsy. The surgeon needs to work closely with the radiologist and the pathologist to arrive at a diagnosis. Once cancer is diagnosed the surgeon then needs to discuss management options with the patient based on a clinical assessment of the stage of disease. Delayed presentation is a problem especially in the more rural parts of Malaysia. With advanced cancers, the diagnosis is easily arrived at; however persuading the patient to have treatment can be a problem. About 10% of patients will try alternative treatment first before finally deciding that it is not working and agree to conventional treatment.

It is important for the surgeon to early on in the consultation to decide who is the decision-maker. Often, the patient herself may not have autonomy in decision making. In women with early breast cancer who are suitable for breast conserving surgery, a patient decision aid giving all the pros and cons of each treatment option, in a language that can be understood by the patient is important. However some patients do not want to take the responsibility for decision making and leave it to the surgeon to decide.

Patient education materials in the clinic are useful to show a woman what a mastectomy looks like compared to a breast conserving surgery. If a mastectomy is required, photos of immediate and delayed breast reconstruction are also shown to the patient.

For clinically Stage 1 and 2 breast cancer, surgery is the preferred primary treatment. Once the pathology report is ready, the patient is discussed in a multidisciplinary meeting, and adjuvant chemotherapy, radiotherapy, hormone therapy, and targeted therapy is recommended based on national guidelines; the patient needs to know the benefit obtained from each modality of treatment. For expensive therapy not covered by the public hospital, discussion of the cost of each treatment is also important.

For women presenting with advanced breast cancer, chemotherapy first have the advantage of determining response to systemic treatment and hence prognosis. Surgery can be carried out later. Fears of the side effects of chemotherapy need to be addressed.
Along the whole journey of the patient with breast cancer, emotional support, peer support and sometimes financial support is important, and above all, good communication between patient and doctor will improve compliance to treatment.

SY04-1

PREDICTION OF LOCAL RECURRENCE ON PREOPERATIVE MRI

Nariya Cho

Dept. of Radiology, Seoul National Univ. Hospital, Korea

Since breast-conserving surgery and adjuvant radiation therapy has been the standard local management strategy for women with early stage breast cancers, ipsilateral breast tumor recurrence (IBTR) has been reported to occur in 7.5-19.3% of patients who had undergone breast-conserving surgery and radiation therapy [1, 2]. Recently, the Early Breast Cancer Trialists' Collaborative Group reported that the use of radiation therapy decreased the 15-year breast cancer death by about a sixth in addition to cutting the rates of local recurrence in half [3]. Because the risk reduction from radiation therapy varies substantially depending on clinicopathologic factors, the patient age, tumor size, nodal status, histologic grade, surgical margin status, and lymphovascular invasion are usually considered for individualized management decisions[4]. Other recent considerations are the basal-like and human epidermal growth factor receptor-2 (HER-2) molecular subtypes which have been reported to be associated with increased risk for IBTR [5, 6].

Nonetheless, IBTR remains an ongoing clinical problem for women undergoing breast-conserving treatment and further investigation to optimize personalized risk assessment is still underway. In terms of imaging biomarkers, a recent study reported that high mammographic breast density greater than 75 % was an independent predictor associated with locoregional recurrence (hazard ratio, 6.6; 95% confidence interval, 1.6-27.7; p=0.01) in breast cancer patients who underwent breast-conserving treatment [7]. The level of background parenchymal enhancement on MRI has also been reported to predict breast cancer risk in a screening population [8]. Although there are differences in the inclusion criteria and study design of these studies, their results all favor the results of extensive basic research that have noted the importance of the microenvironment in the disease progression from benign disease to invasive cancer [9].

In our institution, dynamic contrast enhanced breast MRI has been routinely used for the preoperative evaluation of breast cancer patients since 2004. Thus, we were able to evaluate the association between the parenchymal enhancement feature around the tumor on preoperative MRI and subsequent breast tumor recurrence for the 133 patients with invasive cancers and 215 patients with DCIS [10,11]. We found that a higher parenchymal signal enhancement ratio was an independent factor associated with IBTR in multivariate analysis. Moreover, the odds ratio of signal enhancement ratio was larger than those of omission of radiation therapy or endocrine therapy.

This lecture will be focused on results of our studies and brief review from a radiologist's perspective on research regarding an association between tumor environment and progression.

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SY04-2

SURGICAL ISSUES ACCORDING TO BREAST CANCER SUBTYPES

Woochul Noh

Dept. of Surgery, Korea Cancer Center Hospital, Korea

Patients who develop locoregional recurrence (LLR) have a substantially worse overall survival. For many years, disease burden and type of local treatment were thought to be the primary factors for the risk of LLR after following breast cancer surgery. Now there is an increasing body of evidence that molecular subtype is an important determinant of LLR. Several retrospective studies and a few meta-analysis have indicated the followings;

1. Patients with a non-triple negative (TN) breast cancer were less likely develop LLR than those with a TN tumor after either breast conserving therapy (BCT) or mastectomy.
2. Among patients who underwent BCT, those with Luminal tumors were less likely develop LLR than those with HER2 overexpressing tumors or TN tumors; patients with HER2 overexpressing tumors had a higher risk of LLR than those with TN tumors.
3. Among patients who underwent mastectomy, those with luminal tumors were less likely develop LLR than HER2 overexpressing or TN tumors; there was no difference in LLR between HER2 overexpressing and TN tumors.
4. There was no significant difference in the risk of LLR following BCT in patients with Luminal A (ER+/PR+/HER2-) compared to Luminal B (ER+/PR+/HER2+) breast tumors; Among patients who underwent mastectomy, those with Luminal A tumors were less likely develop LLR than any of other subtypes.
5. There was a lower LLR following mastectomy compared to BCT for Luminal and HER2 over expressing tumors but no differences in LLR was observed between BCT and mastectomy for TN tumors.

These findings indicate that breast cancer biologic subtype is associated with difference in LLR in breast cancer patients treated with BCT or mastectomy. The risk of LLR can be modifies by systemic therapy such as chemotherapy, endocrine therapy and target therapy. For example, the 3-year local recurrence rate was reduced from 7% to 1% by the adding adjuvant trastuzumab to adjuvant chemotherapy in patient cohorts at Memorial Sloan-Kettering Cancer Center.

Although it is uncertain that the type of surgery can modify the risk of LLR, breast cancer biologic subtype should be taken into account when planning ongoing surgical management such as the extent of resection and axillary surgery.

SY04-3

RADIOTHERAPY AFTER BREAST RECONSTRUCTION

Su Ssan Kim

Dept. of Radiation Oncology, Univ. of Ulsan; ASAN Medical Center, Korea

While breast conserving therapy (BCT) which means lumpectomy followed by irradiation of whole breast showed psychosocial advantages compared to mastectomy, but significant portion of patients still undergo mastectomy in association with the tumor size, location, and biology. Studies for quality of life reported that breast reconstruction after mastectomy had psychological advantages than mastectomy alone.

Breast reconstruction can be performed in conjunction with mastectomy using breast implants, autologous tissue or a combination. Breast reconstruction can also be divided into “immediate” (at the same time as mastectomy) or “delayed” (at some time following the completion of cancer treatment). Immediate breast reconstruction (IBR) has several advantages over the delayed reconstruction. It provides esthetic and psychosocial benefits by restoring feminity.

On the other hand, post-mastectomy radiation therapy (PMRT) was proved to increase survival rate for patients with loco-regionally advanced breast cancer in several randomized studies. Despite the oncological benefit of PMRT, it was reported that PMRT after breast reconstruction resulted in significant morbidities. Acute effects occurring over days to weeks usually involve acute inflammatory changes. The delayed response, which can occur from months to years, involves atrophy, fibrosis, and inhibition of normal wound-healing mechanism. PMRT after immediate implant reconstruction resulted in increased rate of capsular contracture. Radiation therapy after autologous tissue reconstruction could brought about complications such as fat necrosis and/or poor cosmetic results.

When PMRT is required, delayed reconstruction is generally preferred after completion of PMRT in autologous tissue reconstruction. But some experienced breast cancer teams reported acceptable results of protocols in which PMRT was performed after immediate reconstructions especially with autologous flaps.

At our department, 79 patients received PMRT after IBR from 1999-2008. Most patients were Stage III (92%). Five-year local control rate was 90.6%. Complications which required surgical interventions developed at 9 cases (11.4%). Of those 1 case received flap removal and reconstruction operations due to flap necrosis. Subgroup analysis was performed to evaluate cosmetic results. Of 62 patients in which cosmetic evaluation was conducted for more than 12 months by a single investigator, 81% of patients showed excellent to good cosmesis. Satisfactory cosmesis was sustained in 76% of patients (25 out of 33 patients) 2 years after radiation therapy. Such factors as poor cosmesis before RT, fat necrosis before RT, chemotherapy, radiation boost were associated with unsatisfactory cosmetic results.

In summary, PMRT can be applied to high-risk breast cancer patients without compromising cosmetic results especially after autologous flap with skilled team approach.

SY05-1

DETECTION AND CHARACTERIZATION OF CIRCULATING TUMOR CELLS

Simon Joosse

Dept. of Tumor Biology, Univ. Medical Center Hamburg-Eppendorf, Germany

Although breast cancer mortality has been steadily decreasing during the last decades due to improvements in early detection and cancer treatment, breast cancer is still one of the leading causes of cancer-related death in women worldwide. Tumor cells that are able to leave the primary tumor, invade the surrounding tissue, and enter the blood circulation, may finally grow out to become metastases in distant organs. Because cancer metastasis is the main cause of cancer-related death, early detection of (micro) metastases is of vital importance. Circulating tumor cells (CTCs) that can be found in a patient's blood, may be used as prognostic markers to estimate the risk for relapse, but also to stratify patients to adjuvant therapy in order to forestall metastasis formation. Furthermore, the detection of CTCs during therapy can be utilized to monitor the efficacy of systemic treatment. Last, investigation of the CTCs may reveal potential therapeutic targets to which the tumor and metastases may respond best.

In order to detect the few rare malignant cells in several milliliters of blood containing billions of red blood cells and tens of millions of leukocytes, extremely sensitive and specific methods are required that are able to process the large amount of cells in a relatively short period of time. Recently, we have developed staining procedures that are able to identify cancer cells based on keratin expression but independent of the epithelial marker EpCAM (epithelial cell adhesion molecule) that might be downregulated during epithelial-to-mesenchymal transition (EMT). EMT is a dedifferentiation process that is thought to be responsible for the first step in the metastatic cascade by allowing cells to become motile via downregulation of adhesion molecules. Compared to the conventionally used keratin antibodies, we were able to successfully detect more circulating tumor cells (CTCs) in blood and show the clear prognostic value of the optimized detection method. Because tumor cells capable of undergoing EMT have the biggest adaptive capability, it is most likely that they also possess the highest probability to form metastases. This underlines the importance of using a broad range of markers to capture as many tumor cells as possible.

Additional to the improved CTC detection method, recent advances in whole genome amplification technology have made it possible to reproducibly amplify the whole genome of single cells. We could show that amplified DNA from single cells lends itself perfectly for mutation and copy number analyses. Our results show that we can reproducibly obtain the whole genome copy number profile of single cells from the breast cancer cell-line SKBR3 that is similar to the copy number profile obtained by array Comparative Genomic Hybridization (CGH) from full genomic DNA of the same cell.

SY05-2

BREAST CANCER BONE METASTASIS – FROM MOLECULAR INSIGHTS TO NOVEL THERAPEUTICS

Yibin Kang

Dept. of Molecular Biology, Princeton Univ., U.S.A.

Bone metastasis is a frequent occurrence in breast cancer, affecting more than 70% of late stage cancer patients with severe complications such as fracture, bone pain, and hypercalcemia. The pathogenesis of osteolyitc bone metastasis depends on cross-communications between tumor cells and various stromal cells residing in the bone microenvironment. Using in vivo imaging technology, we showed that TGFβ is released from bone matrix upon bone destruction, and signals to breast cancer to further enhance their malignancy in developing bone metastasis. We furthered identified Jagged1 as a TGFβ target genes in tumor cells that engaged bone stromal cells through the activation of Notch signaling to provide a positive feedback to promote tumor growth and to activate osteoclast differentiation. More recently, we identified tumor-induced osteoclast miRNA as regulators and biomarkers of osteolytic bone metastasis. Importantly, pharmaceutical inhibitors against these signaling pathways reduce the development of bone metastasis, suggesting novel avenues for clinical management of skeletal complications of breast cancer.

SY05-3

BREAST CANCER AND METASTASIS: ON THE WAY TOWARD INDIVIDUALIZED THERAPY

Jean Paul Thiery*

Dept. of Biochemistry, School of Medicine, National Univ. of Singapore, Singapore

Breast cancer is one of the leading causes of death in females worldwide, with an increasing frequency in Asia in part due to a progressive shift toward a westernized lifestyle. Expression profiling of breast cancers has led to the identification of five molecular subtypes, classified as Luminal A, Luminal B, Her2, Basal and Claudin-low. This molecular classification complements the well-established clinicopathological stratification, which includes the ER, PR and HER2 status, grading and staging. However, these parameters and different expression profile signatures remain only indicators of prognosis and do not permit an accurate assessment of the patients' response to treatment (Bidard et al., 2013). Metastasis of breast cancer is life-threatening and the mechanisms driving this process are not yet fully elucidated. Recently, the phenotyping of breast cancer Circulating Tumor Cells (CTCs) has begun to deliver some critical information pertaining to breast cancer, with considerable heterogeneity observed. This finding and the mutational landscape of different breast cancers have reinforced the idea that breast cancer is a constantly evolving malignant disease, generating multiple clones and thus favouring resistance to conventional and targeted therapeutics. Over a decade ago, the hypothesis was made that Epithelial-Mesenchymal Transition (EMT) may have been co-opted by carcinoma cells to invade the local environment, intravasate and disseminate to distant organs, while its reverse mechanism, Mesenchymal-Epithelial Transition, may operate at secondary sites to generate clinically detectable metastases (Thiery, 2002). EMT is a fundamental mechanism governing morphogenesis that employs multiple signaling pathways to shape the embryo (Lim and Thiery 2012). The intriguing possibility that EMT operates in carcinomas is now documented in experimental models, with the discovery of mesenchymal phenotypes in tumor subsets. In addition, the transition of an epithelial carcinoma into a mesenchymal-like state is potentially associated with increased stemness, therapeutic resistance, and immune escape. We shall first present data to describe EMT scoring of the different breast molecular subtypes and their cell line counterparts.

The phenotype of CTCs has been explored in vitro following expansion in short-term culture (Khoo et al., 2013). A number of CTCs express EMT markers consistent with other recent studies (Thiery and Lim, 2013). In addition, the potential for CTCs to transiently expand in vitro may provide a surrogate marker for patient response to neoadjuvant therapy. Our current strategy is aimed at designing new therapeutic approaches using drug combinations that interfere with the plasticity of breast and other carcinoma cells, with the ultimate hope that the reversal to a more epithelial phenotype will improve the response of carcinoma cells to conventional cytotoxics. A preliminary, high-content screening assay, using a carcinoma cell line that is able to undergo EMT following exposure to growth factors (Chua et al., 2012), was designed to simultaneously analyze both cell growth and cell migration via time-course imaging in multi-well plates. Using this assay, we validated several compounds as viable EMT inhibitors. In particular, we have identified compounds targeting ALK5, MEK and SRC as potent inhibitors that can interfere with EGF-, HGF- and IGF-1-induced EMT signaling.

We have recently developed a 3D screen to interfere with EMT triggered by endothelial cells organized as a vessel in a microfluidic device. This system delivers a more accurate representation of the in vivo situation (Aref et al., 2012; Bai et al., in preparation). We also examined the contribution of EMT to immune escape in the breast cancer MCF7 cell model system (Akalay et al., 2013). Our results show that MCF7 cells rendered mesenchymal by the forced expression of Snail or by a chronic exposure to TNF-α become refractory to a specific cytotoxic T lymphocyte (CTL) clone. This CTL clone forms a functional immune synapse with wild-type MCF7 cells in contrast to EMTed cells which acquire a drastically modified cortical actin cytoskeleton. The loss of response is in part linked to the activation of an autophagy program. Our studies collectively emphasize a role for EMT in the progression of breast carcinoma. However we must remain cautious until one shall definitively provide clinical evidence for the use of EMT as global surrogate descriptor of invasive and metastatic phenotypes and that targeted therapeutics could be effectively able to modify these phenotypes and render carcinoma more susceptible to conventional chemotherapy and immune response (Thiery and Sleeman 2006; Thiery et al., 2009).

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<Co-Authors>
Bee Luan Khoo[1], Prashant Kumar[2], Sim Wen Jing[2], Kelvin Chua[3], Tuan Zea Tan[3], Intissar Akalay[4], Salem Chouaib[4], Fathia Mami-Chouaib[4], Bassam Janji[5], Masaaki Matsuura[6], Seiichi Mori[7], Boon Cher Goh[8], Soo Chin Lee[8], Amir Aref[9], Ting-Yuan Tu[9], Bai Jing[9], Roger Kamm[10] and Chew Teck Lim[11]

[1] Mechanobiology Institute, National Univ. of Singapore, Singapore
[2] Institute of Molecular and Cell Biology, Singapore
[3] Cancer Science Institute, National Univ. of Singapore, Singapore
[4] Unite INSERM U753, Institut de Cancerologie Gustave Roussy, Villejuif, France
[5] Dept. of Oncology, Public Research Center for Health (CRP-Sante), Luxembourg, Belgium
[6] Division of Cancer Genomics, Cancer Institute of Japanese Foundation for Cancer Research Tokyo, Japan
[7] Cancer Science Institute, National Univ. of Singapore; Division of Cancer Genomics, Cancer Institute of Japanese Foundation for Cancer Research Tokyo, Japan, Singapore
[8] Cancer Science Institute; Dept. of Hematology-Oncology and Pharmacology, National Univ. Hospital, Singapore,
[9] BioSystems and Micromechanics (BioSyM) IRG, Singapore-MIT Alliance for Research and Technology (SMART) Centre, Singapore
[10] BioSystems and Micromechanics (BioSyM) IRG, Singapore-MIT Alliance for Research and Technology (SMART) Centre; Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, U.S.A.
[11] Mechanobiology Institute; BioSystems and Micromechanics (BioSyM)IRG, Singapore-MIT Alliance for Research and Technology (SMART) Centre; Dept. of Bioengineering and Mechanical Engineering, NUS, Singapore

SY06-1

ONCOGENIC PIK3CA MUTATIONS: TARGETED THERAPIES AND DIAGNOSTICS

Ben Ho Park

Dept. of Oncology, Johns Hopkins Univ., U.S.A.

Cancer genome sequencing has revealed a number of potential therapeutic targets based upon somatic oncogenic changes in key genes and pathways. An essential component for translating these discoveries for therapeutic benefit is validating somatic alterations, such as mutations, as functional or "driver" mutations. Once validated, drug development against the target can lead to highly effective therapies. However, having companion molecular diagnostic assays has become critical in identifying patients with the highest likelihood of response, that is, patients that have cancers harboring the somatic alteration. Until recently, the concept of tumor heterogeneity leading to potential misinformation regarding a patient's cancer mutational profile was underappreciated.

PIK3CA is an oncogene encoding the catalytic subunit of PI3 kinase alpha. In 2004, our lab first identified that this gene was mutated at high frequency in breast cancers with three recurrent "hotspot" mutations comprising the majority of mutations found in human malignancies. Several years later, our group demonstrated using somatic cell gene targeting that "knock in" of these hotspot mutations within non-cancerous human mammary epithelial cell lines led to features of transformation, thus validating these mutations as functionally significant and targets for therapy. Using these isogenic models, we and others have established cell based screening to identify PI3 kinase inhibitors. In addition, we have also developed digital PCR assays to detect these mutations in blood, providing a "liquid biopsy" for patient selection in future trials. These translational aspects of oncogenic PIK3CA mutations will be discussed.

SY06-2

HOW CAN WE OVERCOME PI3K ACTIVATION? -EMERGING PI3K INHIBITORS

Cristian Massacesi

Dept. of Oncology Global Development, Novartis Pharmaceutical, France

Multiple components of the PI3K pathway are often dysregulated in cancer cells and over-activation of PI3K signaling is implicated in many aspects of tumor growth and survival. Activation of this pathway can be the result of: i) Amplification and/or overexpression of the p110α catalytic subunit; ii) Presence of activating mutations in the PIK3CA gene encoding the p110α catalytic subunit; iii) Constitutively active mutants or overexpression of receptor tyrosine kinases (e.g. EGFR, ErbB2) leading to constitutive recruitment and activation of PI3K; iv) Constitutive recruitment and activation by mutant forms of the Ras oncogene; v) Loss or inactivating mutation of the tumor suppressor gene PTEN, a endogenous negative regulator of the PI3K pathway; or vi) Overexpression of the downstream kinase Akt.

Preclinical work suggests that inhibition of the PI3K signaling pathway might provide benefit for the treatment of many solid tumors and breast cancer specifically. Therefore, therapeutic interventions on PI3K signaling could represent a rationale approach for the treatment of breast cancer and could, in addition, increase the efficacy of already established antineoplastic treatments like cytotoxic agents, endocrine agents, targeted agents, etc.

Currently a large number of PI3K and Akt inhibitors are being investigated in clinical trials. Despite strong scientific rationale and supportive preclinical data, a consistent limited single agent clinical activity has been reported to date for most of these compounds. Nevertheless, interesting preliminary clinical data are emerging when this class of compounds are combined with other antineoplastic agents (e.g., with hormonal agents). These emerging data suggest that targeting the overactivated PI3K pathway may be critical to overcome drug-resistance and may provide clinical benefit.

With regards to biomarker strategy, the complexity of PI3K/Akt pathway and the high number of key players in the pathway has thus far limited the profiling of biomarkers which can guide the pre-identification of patients most likely to benefit from PI3K inhibition.

An overview on the challenges faced and the strategy implemented in the clinical development of PI3K inhibitors in breast cancer will be discussed, using as example Novartis compounds buparlisib (BKM120), a PI3K pan-class I (isoforms α, β, γ, δ) inhibitor, and BYL719, a selective of p110α catalytic isoform inhibitor.

SY06-3

TARGETING MTOR PATHWAY: CLINICAL IMPLICATION IN THERAPY

Janice Tsang

Dept. of Clinical Oncology, Queen Mary Hospital; The Univ. of Hong Kong, Hong Kong

The PI3K/AKT/mTOR pathway is an established oncogenic driver in humans. The mammalian target of rapamycin (mTOR) is a downstream mediator in the PI3K/AKT signaling pathway and plays a critical role in cell survival. It is a serine-threonine kinase that is a master regulator of protein synthesis, with its mTOR activity in the cell being carried out by two distinct complexes: 1) the mTORC1 complex, which is very sensitive to rapamycin and activates S6K and inactivates 4E-BP1, leading to protein translation and cell growth; 2) the mTORC2 complex which is less sensitive to rapamycin, and its role in normal cell function and oncogenesis has not been well understood. However, it is known to activate AKT, thereby promoting cell proliferation and survival. Over the years, there have been emerging randomized phase III studies demonstrating the efficacy of agents targeting the PI3K/AKT/mTOR axis, leading to the approval of various mTOR inhibitors, such as everolimus and temsirolimus, showing added value in the clinical outcome for solid tumours.

Breast cancer is a heterogeneous disease. About 60-70% of all breast cancer patients are hormone-positive and this subtype of breast cancer initially tends to show a high overall response rate to hormonal treatments. However, endocrine resistance eventually develops, leading to tumour progression. It is known that high activation level of the PI3K/AKT/mTOR pathway is related to endocrine resistance as well as resistance towards conventional chemotherapy. Furthermore, the efficacy of mTOR inhibitors has also been ascribed to the involvement of the mTOR pathway in tumor-related angiogenesis. The use of mTOR inhibitors in breast cancer is not the only means of treatment of endocrine resistant tumours. Various strategies are under development to combine mTOR inhibitors, with hormonal therapies, and these combinations are anticipated to enhance the efficacy of currently available endocrine treatment options.

This lecture is going to give an overview on the role of mTOR pathway in the tumour progression of breast cancer, relating pre-clinical data for mTOR inhibitors with summary of the recent clinical trials showing the efficacy of various strategies using the mTOR inhibitors. The safety profile of the therapeutic agents will also be discussed, and updates of on-going studies for future directions will also be presented.

SY07-1

CHANGING TREATMENT PARADIGM OF HER2 POSITIVE BREAST CANCER: CLINICAL APPLICATION OF NEW AGENTS

Seock-Ah Im

Dept. of Internal Medicine, Seoul National Univ. Hospital, Korea

Metastatic breast cancer (mBC) treatment was depending on cytotoxic chemotherapy for long time. However, over the past twenty years, treatment has evolved to a more target-directed approach. We now employ tailored therapy based on the presence or absence of estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2).

Amazing dream comes true in HER2+ mBC. Targeting different portions of the HER signaling pathway are in various stages of development. Notably, pertuzumab, a humanized monoclonal antibody that binds to a dimerization domain of the extracellular portion of the HER2 receptor, was recently approved for use in HER2+ mBC as 1st line therapy in US and EU. Trastuzumab binds to the extracellular domain IV of HER2, which results in the down-regulation of the PI3K/Akt pathway. Pertuzumab efficiently inhibits ligand-induced HER2/HER3 dimerization, whereas trastuzumab has only a minor effect in the presence of a ligand. Combination therapy with pertuzumab plus trastuzumab may results in more comprehensive blockade of HER2 signaling than can be achieved with trastuzumab alone [1-3].

CLEOPATRA is a phase III study to compare the efficacy and safety of pertuzumab, trastuzumab, and docetaxel with placebo, trastuzumab, and docetaxel in patients with HER2-positive first-line mBC. The results of the primary analysis showed significantly longer median progression-free survival in the pertuzumab group (18.7 months) than in the placebo group (12.4 months) (hazard ratio 0.69, 95% CI 0.58-0.81). Median overall survival was 37.6 months (95% CI 34.3-NE [not estimable]) in the placebo group but had not been reached (95% CI 42.4-NE) in the pertuzumab group (hazard ratio 0.66, 95% CI 0.52-0.84; p=0.0008) [4, 5]. Lapatinib, a small-molecule tyrosine kinase inhibitor was currently prescribed for HER2 + mBC who failed anthracycline, taxnae and trastuzumab. Trastuzumab emtansine (T-DM1) is a human epidermal growth factor receptor 2 (HER2)-targeted antibody-drug conjugate (ADC) composed of trastuzumab, a stable thioether linker (MCC), and the cytotoxic agent DM1 (derivative of maytansine). The phase III randomized trial EMILIA has shown that T-DM1 provided better objective tumor responses and significantly improved PFS and OS compared to lapatinib and capacitabine in HER2+ mBC with a prior taxane and trastuzumab regimen[6]. Recently published randomized, open-label, first-line trial comparing trastuzumab and docetaxel with single agent T-DM1 showed a significant improved PFS for T-DM1[7]. The ongoing phase III trials MARIANNE and TH3RESA will further give information about the place of T-DM1 in the treatment algorithms for HER2+ mBC.

In summary, pertuzumab, lapatinib, and T-DM1 may offer better chance to prolong overall survival of HER2 positive mBC. There are ongoing studies showing an increasing tendency towards moving these agents to earlier stages of HER2-positive breast cancer.

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SY07-2

BRAIN METASTASES IN HER2-POSITIVE BREAST CANCER PATIENTS

Yoon Sim Yap

Dept. of Medical Oncology, National Cancer Centre Singapore, Singapore

The advent of new systemic therapies has led to an unprecedented improvement in treatment outcomes for HER2-positive breast cancers. Brain metastases, however, still present a major challenge. The incidence of brain metastases is increased in patients with HER2-positive breast cancers compared to other subtypes. The prognosis of patients with brain metastases depends on a number of factors, including age, performance status, number and site of brain metastases, extent of extracranial disease. Although most studies on brain metastases from breast cancer have been conducted in Western countries, we will review some of the data from Asian countries on the epidemiology and treatment outcomes.

Local therapy remains the standard of care as initial therapy for most patients with brain metastases. In the setting of solitary brain metastasis, surgery or stereotactic radiosurgery(SRS) followed by whole-brain radiotherapy(WBRT) may confer better outcomes compared to WBRT alone. WBRT is the mainstay treatment for patients with multiple brain metastases. There is an unmet need for better systemic therapies for brain metastases, as recurrence or progression of brain metastases is a major cause of morbidity and mortality.

At present, the role of systemic therapies for brain metastases from breast cancer is not well established. This is an evolving area of research. Only selected anti-cancer drugs can permeate an intact blood-brain barrier (BBB). However, the BBB may be compromised with the development of brain metastases and radiotherapy. There are anecdotal reports of efficacy with various chemotherapeutic regimens, but there is limited data from prospective trials of chemotherapeutic regimens. Patients with uncontrolled brain metastases are excluded from most clinical trials. Recent trials support the efficacy of lapatinib-based regimens in the treatment of HER2-positive brain metastases. Limitations of these studies include the nonrandomised design and relatively small patient numbers for most of them. There is also a need to standardise response criteria; the standard RECIST criteria is not ideal for the assessment of brain metastases.

Improved understanding of the biology of brain metastases will help in the development of novel treatment strategies. Currently, there are ongoing clinical trials to evaluate the efficacy of therapies targeting HER2, VEGF, mTOR, PI3K and LRP-1.

SY07-3

DETERMINANTS OF RESISTANCE TO TRASTUZUMAB IN ADJUVANT SETTING

Soonmyung Paik

Division of Pathology, National Surgical Adjuvant Breast and Bowel Project(NSABP) Foundation, Inc., U.S.A.

Four large randomized clinical trials have clearly demonstrated the clinical efficacy of trastuzumab in adjuvant setting when added to or administered after standard chemotherapeutic regimen. There is a growing need to identify a subset of HER2 positive patients with high residual risk after adjuvant trastuzumab as a result of the success of dual targeted approaches such as trastuzumab-pertuzumab combination in neoadjuvant and advanced disease setting. In theory, high residual risk after adjuvant trastuzumab could be the results of either resistance to trastuzumab or high baseline risk that cannot be completely overcome by benefit from trastuzumab despite the absence of resistance. Therefore investigations of both resistance phenotype and prognostic factors are of clinical interest.

The biological determinants of the degree of benefit from adjuvant trastuzumab seem to be complex. Cancer stem cells isolated from luminal subtype breast cancer cells expressed high levels of HER2 protein and were susceptible to trastuzumab therapy. Furthermore bone metastases of breast cancer frequently overexpressed HER2 protein in the absence of ERBB2 gene amplification presumably induced by RANKL secreted by osteoblasts. Disseminated cancer stem cells or bone micro-metastatic cells may be susceptible to trastuzumab treatment regardless of the HER2 status of the primary tumor.

In line with these preclinical and clinical observations, we have previously reported that in B-31 trial conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP), even patients diagnosed with HER2 negative tumors may benefit from adjuvant trastuzumab. Subsequently we developed and confirmed a predictive gene expression signature which identified a subset of B-31 patients with no benefit from trastuzumab that were characterized by high level expression of ER related genes (ESR1, CA12, GATA3, IGFR1, NAT1) in the presence of moderately high level expression of HER2 amplicon genes (ERBB2, GRB7, C17orf37) in their tumors. Intriguingly but in agreement with previous clinical report, clinically HER2 negative tumors identified by central HER2 assays belonged to the mRNA subset that derived benefit from adjuvant trastuzumab rather than to the resistant subset.

Although confirmed, predictive gene expression signature developed from B-31 trial classified only ~10% of clinical HER2 positive tumors to the subtype with no benefit from trastuzumab and more importantly failed to identify a subset with high residual risk after trastuzumab.

Therefore further investigation of clinical association of various molecular subtypes within clinically HER2 positive tumors is required. In this talk, results of the testing for two candidate markers - PAM50 intrinsic subtypes and PIK3CA mutation will be discussed.

1) PAM50 intrinsic subtypes

The Cancer Genome Atals (TCGA) data demonstrated that only ~50% of clinically HER2 positive breast cancer is classified as HER2 Enriched (HER2E) mRNA subtype with rest classified largely as luminal mRNA subtypes, and some of the HER2 negative tumors are classified as HER2E. According to the integrated analysis of DNA copy number, mRNA, and protein expression data, HER2E tumors are characterized by high protein and phospho-protein expression of EGFR and HER2 in addition to co-overexpression of genes within ERBB2 amplicon.

Based on TCGA data, it seems reasonable to predict that response to HER2 targeted therapies may be largely restricted to HER2E subtype regardless of clinical HER2 status. In support of this reasoning, in retrospective analysis of pretreatment core biopsy specimens from CALGB 40601 trial, 80% of HER2R tumors had complete pathological response (pCR) compared to 25-32% pCR in other subtypes upon treatment with neoadjuvant trastuzumab chemotherapy combination. If this finding can be extrapolated to adjuvant setting, DFS gain from adding trastuzumab to adjuvant chemotherapy would be largely limited to HER2E subtype defined by PAM50 assay. On the other hand, if the benefit from adjuvant trastuzumab is largely dependent on response of cancer stem cells or disseminated tumor cells with HER2 status different from the primary tumor, the association between HER2E mRNA subtype and response to trastuzmab observed in neoadjuvant setting may not hold true in adjuvant setting.

Since all PAM50 genes were included in the B-31 dataset, we tested the statistical interaction between HER2E subtype and the degree of trastuzumab benefit.

2) PIK3CA mutation/PTEN loss

Signaling to PI3K-Akt as a result of HER2-HER3 dimerization is regarded as the most important survival pathway downstream of HER2. Several lines of evidence suggest that inhibition of PI3K-Akt is critical for the antitumor effect of HER2-directed therapies. Indeed, several of the proposed mechanisms of resistance to trastuzumab involve persistence or reactivation of PI3K signaling via alternative amplified receptor tyrosine kinases and/or mutations in PI3K pathway components, thus suggesting that direct and more sustained inhibition of PI3K might be a strategy to overcome or prevent resistance to trastuzumab or other HER2 inhibitors.

While a study using global knock out screen of a single HER2 amplified breast cancer cell line demonstrated PIK3CA mutation or PTEN loss as a potential mechanism of resistance to trastuzumab, many ERBB2- amplified cell lines were highly sensitive to PIK3CA siRNA regardless of the presence or absence of mutations in PIK3CA gene in a global knock out screen of many cancer cell lines and additive effect of combining trastuzumab with PIK3CA inhibitor was observed in both trastuzumab sensitive and resistant cell lines, suggesting that signaling through multiple pathways converge on PI3K in HER2 positive cancer cells and supporting the clinical development of PI3K pathway (PIK3CA, AKT, mTOR) inhibitors in ERBB2-dependent breast cancer regardless of PIK3CA mutation status.

However, toxicity of PI3K pathway inhibition may limit its clinical utility and selection of the right subset in HER2 positive breast cancer that is the best candidates for testing the combination regimen is an important clinical question.

Activating mutations in PIK3CA gene or loss of PTEN expression have been proposed as the most important markers of PI3K pathway activation that lead to resistance to trastuzumab. The clinical implication of the latter hypothesis is that clinical development of PI3K inhibitors should be focused on patients with tumors that have either PIK3CA mutation or PTEN loss. Indeed several clinical studies using tumor tissue from either advanced disease or neoadjuvant setting demonstrated such an association, but other studies failed to replicate the association. Recent meta-analysis of the published studies failed to confirm the interaction between PIK3CA mutation or PTEN loss and resistance to

trastuzumab. Furthermore retrospective analyses of FINHER and N9831, two randomized clinical trials of adjuvant trastuzumab, did not find any trend suggesting the role of either PIK3CA mutation (FINHER) or PTEN loss (N9831) in trastuzumab resistance.

We conducted retrospective mutation analyses of randomly selected subset of patients enrolled in B-31 study. Data from these two investigations do not support the role of PAM50 intrinsic subtypes orPIK3CA mutation as a determinant of resistance to trastuzumab in adjuvant setting.

SY08-1

UNDERSTANDING DIETARY ISSUES AND MODIFICATIONS FOR BREAST CANCER SURVIVORS: INSIGHTS FROM HEALTH CARE PROVIDERS AND SURVIVORS

Katherine Clegg Smith

Dept. of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, U.S.A.

As of 2011, 2.6 million women in the United States were living with a history of breast cancer. Great progress has been made in preventing and treating breast cancer. Unfortunately, survivors still face elevated risks for cancer recurrence, a second cancer, and chronic diseases, such as cardiovascular disease and diabetes. Engaging in healthy lifestyle behaviors, including maintaining a healthy weight and diet and increased physical activity, have been proposed as strategies for reducing health risks. Most breast cancer survivors do not meet current lifestyle behavioral recommendations, and there is limited research exploring current practices and feasibility of implementing effective behavior change interventions. To begin to fill this gap, we employ a detailed, mixed methods research method that gives voice to both survivors and members of cancer care teams.

We present data from a mixed methods study of diet among long-term cancer survivors in the mid-Atlantic region of the USA. In the study's first phase, we conducted key informant interviews with members of cancer care teams in which they articulated their perspectives on the barriers and facilitators to healthy behaviors faced by their patients. In phase 2, we recruited women who had been diagnosed with cancer at least 3 years ago and who had completed active treatment. Over the course of one month (4 contacts) women completed three 24-hour dietary recalls, and provided data on physical activity, tobacco use, and quality of life. In addition, we conducted two qualitative interviews with each woman in which we explored identity issues and the relevance of 'survivor' to self concept. In the interviews, women described their cancer and treatment experiences and articulated breast cancer's relevance to their self concept and current quality of life, and their understanding of their diet in health-related terms. We integrate data from both clinicians and survivors on issues related to encouraging, establishing and maintaining healthy diet during and after completion of acute treatment. Our goal is to use insights garnered to inform feasible and effective lifestyle interventions to ensure health throughout the survivorship trajectory.

NAVIGATING FAMILY ISSUES WITH BREAST CANCER

Frances M. Lewis

Dept. of Family and Child Nursing, Univ. of Washington, U.S.A.

Cancer invades and causes ripple effects in the family.[1]

Families matter. They matter because they form the first line of support to the patient with breast cancer. They also matter because they are directly impacted by cancer-related pressures and are often on their own to understand the disease and treatment, how to help the patient manage, how to correctly interpret the patient's symptoms, and how to maintain some semblance of balance between family life and life with the breast cancer. Increasingly we have come to learn that cancer threatens the core functions of a household family, even high functioning families.[2, 3] Cancer can take over the family's life at the expense of maintaining nurturing and caring interpersonal communication, quality parenting, and supportive marital communication. [3,4,5,6]

Families suffer unnecessarily when cancer is diagnosed, when it recurs, or when it moves to an advanced stage. General advice or broad-stroke help from professionals is not sufficient. Printed material is not sufficient to help. Targeted, planned, systematic professional services are needed to help families deal with their "stuck points," the cross-cutting issues that are known from research to affect how a family experiences, adjusts, and functions when a family member has cancer.

There are 3 purposes to this presentation: 1. to analyze breast cancer as a family illness, not a patient's disease; 2. to describe "stuck points" spouse caregivers and children experience in adjusting to and managing the wife or mother's breast cancer; and 3. To describe 2 behavioral intervention programs that are known from research to improve adjustment and functioning in the diagnosed patient, her spouse caregiver, and her children. What is ultimately needed in provider settings is family-focused care that helps families thrive, not merely survive, the breast cancer.

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SY08-3

POST TREATMENT : PERSONAL INSIGHT, POLITICAL POTENTIAL

Laura C. Nelson

Gender and Women's Studies, Univ. of California, Berkeley, U.S.A.

The incidence of breast cancer in South Korea is still relatively low, but it is rising rapidly. Moreover, breast cancer in South Korea strikes a younger average demographic group than in most other places: more than half of all newly-diagnosed women in South Korea were under 50 years old. Fortunately, the prognosis for most women diagnosed with breast cancer in South Korea is good, but this means that many survivors now live years in a liminal state between health and mortality. The standard epidemiological associations of lifestyle changes with breast cancer are well-known in South Korea and patients often refer to these as possible causes of their own illness; after treatment, many limit their alcohol consumption and improve the healthfulness of their diets in an effort to reduce the likelihood of recurrence. But traditional Korean understandings of the roots of breast cancer point to stress, which leads some women to consider fundamental changes in their social relationships as critical to the prevention of recurrence. In this talk I discuss the self-reflections of South Korean breast cancer survivors, and the potentially radical critiques of normative expectations for women embedded in their attempts to reduce stress and maintain health. The paper draws on ethnographic observations, qualitative interviews, and cultural analysis.

SY09-1

WHAT IS THE MECHANISM OF HORMONE THERAPY RESISTANCE IN LUMINAL BREAST CANCER?

Matthew J. Ellis

Division of Oncology, Section of Breast Oncology,
School of Medicine, Washington Univ., Siteman Cancer Center, U.S.A.

Many Stage 3 breast cancers and effectively all Stage 4 breast cancers are fatal, with annual worldwide deaths from the disease approaching one-half million (Youlden et al., 2012). The majority of these deaths occur in patients with estrogen receptor positive disease and therefore it can be argued that resistance to endocrine therapy is the most significant clinical problem in breast cancer oncology. Large-scale partial and whole genome sequencing has recently been conducted on early-stage treatment naive breast cancer samples (Cancer Discov 2013; 3: 27-34). By contrast, the genomic landscape of advanced and treatment-resistant breast cancer is poorly documented. We therefore developed a panel of patient-derived xenografts (PDX) from patients with poor prognosis endocrine-resistant disease for genomic and functional studies (Cell Reports 2013 in press). The value of the PDX approach in the setting of estrogen receptor positive (ER+) breast cancer had been questioned because very few breast cancer PDX expressing ER have been reported.

Whole genome sequencing (WGS) using massively parallel techniques was used to compare the originating tumor with six counterpart ER+ PDX examples because partial genome sequencing, focused on coding sequence alone (i.e. exome sequencing), does not fully document all mutations; particularly structural variants (SV) or other mutational events occurring in non-coding space. Heterogeneity in mutation frequencies also has not been comparatively evaluated for PDX models and originating tumors, so a customized capture approach was used to generate high depth at somatic variant positions genome-wide, coupled with statistical analyses for this comparison. RNA sequencing was conducted to determine the expression level of individual mutations and to confirm gene fusion events. Functional analyses were used to reveal mechanistic insights into endocrine resistance that have not been achieved using conventional cell line approaches.

Four of the estrogen receptor positive PDX were associated with ESR1 ligand binding domain mutations (Y537S and E380Q), ESR1 gene amplification or an ESR1/YAP1 translocation. These events produced different endocrine therapy response phenotypes in human, cell line and PDX endocrine response studies. Hence, deeply sequenced PDX models are an important resource for the search for exploring new treatment options in endocrine therapy resistant breast cancer and capture endocrine drug resistance etiologies, i.e. ESR1 gene rearrangements and mutations, not observed in standard cell lines. Currently we are exploring new pharmacological approaches in endocrine therapy resistant PDX models to develop preclinical data for new treatment options for this large group of poor outcome patients.

SY09-2

ENDOCRINE RESISTANCE: IMPLICATIONS FOR ADJUVANT THERAPY IN HER2 NORMAL DISEASE

Hope S. Rugo

Dept. of Medicine, Univ. of California San Francisco Medical Center, U.S.A.

Recent studies have highlighted the heterogeneity of hormone receptor positive breast cancer, with a better understanding of the pathways that drive both acquired and de novo resistance to hormone therapy. Gene expression analyses have differentiated several subtypes of hormone receptor positive disease, and have identified change in proliferation as a potential marker of hormone sensitivity. Activation of the phosphotidyl inositol 3 kinase (PI3K) pathway has been associated with more proliferative and hormone resistant disease, generating intense interest in the use of inhibitors of this pathway as a mechanism for improving response to hormone therapy. mTOR, the mammalian target of rapamycin, is downstream of PI3K, but available inhibitors were both potent and had tolerable toxicity profiles. Although a neoadjuvant study combining letrozole and the mTOR inhibitor everolimus resulted in improved clinical and radiographic response compared to letrozole, a marker predictive of response could not be identified. The phase III Bolero II trial therefore used clinical parameters to identify a patient population most likely to benefit from mTOR inhibition, treating patients with advanced hormone receptor positive cancers that had progressed on nonsteroidal aromatase inhibition with either exemestane and placebo or exemestane combined with everolimus. The addition of everolimus to primarily second line hormone therapy resulted in a significant improvement in outcome by both investigator and independent assessment, more than doubling progression free survival with 18 months median follow-up. At this time, the final survival analysis is pending, but at 18 months there was a trend toward improved survival in patients receiving everolimus. Toxicity was similar to previously reported trials with mTOR inhibitors, including mucositis, rash, and fatigue as some of the more common side effects, and grade 3 interstitial pneumonitis in 3%. These symptoms were generally well managed by dose reduction, interruption, and occasionally discontinuation. The benefit of adding everolimus was seen across all subgroups including patients who had previously received adjuvant therapy, or those with visceral disease. A molecular analysis using next generation sequencing in a subset of tumor samples from Bolero II failed to identify specific predictive markers; all patients appeared to benefit with the exception of a small number of tumors with mutations in multiple pathways.

Newer agents that inhibit PI3K alone or in combination with other kinases are now in clinical trials and have already demonstrated anti-tumor efficacy. In addition, an intriguing story has emerged with cyclin dependent kinases (CDK) 4 and 6 inhibitors. CDK 4 and 6 control the cell cycle by inactivating Rb by phosphorylation, allowing progression from G1 to S phase. The CDK4/6 inhibitor palbociclib was tested in vitro by Finn et al in a number of different cell lines. Finn and colleagues found that this agent had its greatest anti-tumor effect in tumors that were either hormone receptor positive but more proliferative, or in those that were HER2 positive. An interim analysis of a subsequent randomized phase II trial in the first-line advanced disease setting demonstrated a tripling of progression free survival with the addition of palbociclib compared to placebo to hormone therapy with letrozole. The

primary toxicity was bone marrow suppression, with reversible neutropenia managed by intermittent dosing and dose reduction when necessary. A phase III trial with palbociclib is ongoing in the same setting.

What are the implications for adjuvant therapy? The majority of breast cancer expresses hormone receptors, and recurrence can occur for well over a decade from initial diagnosis. We are largely unable to determine which tumors within this subset are more or less likely to respond to adjuvant hormone therapy. Advances in hormone therapy have changed side effect profiles, and improved disease free survival, with a modest at best impact on overall survival. Inasmuch as our goal is to prevent distant recurrence, we need to optimize adjuvant hormone therapy and identify the tumors that will be most likely to require additional interventions. Certainly more highly proliferative disease is of interest, but late recurrence continues to be a significant problem for patients with indolent disease as well. These targeted agents offer the hope of improved outcome, but ongoing and planned studies will need to carefully identify which tumors and patients are most likely to benefit, and pay close attention to quality of life and minimizing treatment toxicity.

GBCC2013

Panel

PN01-1

ROLE OF PREOPERATIVE MRI IN BREAST CANCER

Min Jung Kim

Dept. of Radiology, Yonsei Univ. Severance Hospital, Korea

In oncologic patients, staging of the disease extent is of paramount importance. Magnetic resonance (MR) imaging has demonstrated superior sensitivity for invasive and in situ cancer detection as well as more accurate tumor sizing compared with physical examination, mammography, and ultrasound. Although it seems intuitively obvious that an improved ability to detect cancer would be beneficial, evidence of improved patient outcomes is lacking. Routine use of preoperative MR imaging for patients with newly diagnosed breast cancer has not definitively been shown to improve survival, decrease reexcision rates, or decrease the cost of care.

Given the rapid advances in MR imaging technology with respect to spatial resolution, higher field strength, new coil technology, and the improved capabilities for MR imaging biopsy during the past several years, it is important to continue to assess the utility of breast MR imaging in the preoperative setting. In particular, there are likely specific subpopulations of patients who will benefit from preoperative breast MR imaging. In this talk, I would like to show some promising subpopulations of patients will benefit from preoperative breast MR imaging. And how to improve the diagnostic performance of MR imaging will be discussed.

First, with lobular histologies, additional ipsilateral disease is reported approximately 50% of the time. Furthermore, synchronous contralateral disease is reported in 13% of cases. The data do suggest that preoperative MR imaging for lobular cancers changes surgical management. Change in management based on preoperative MR imaging was reported to occur twice as frequently with lobular cancers than with ductal cancers. But the re-excision rate in patients who underwent preoperative MR imaging was significantly lower than those without preoperative MR imaging.

Second, Posterior tumors are well assessed by MR imaging for the determination of chest wall invasion. For purposes of staging, the chest wall includes the intercostal muscles, ribs, and serratus anterior musculature. Breast MR imaging includes these structures in the imaging field of view, conferring an advantage over mammography. The surgical plan is influenced with chest wall disease, often requiring involvement by the thoracic surgeon. And MR imaging has been shown to be valuable in assessing the response to NAC. Given its high sensitivity, MR imaging has been particularly useful to guide breast cancer surgery by differentiating pathologic complete response from residual tumor after NAC. A recent metaanalysis found that MR imaging accurately detects residual tumor following NAC and is more accurate than mammography in estimating residual tumor burden.

There is less data but some support for preoperative staging in women with dense breasts and women at high risk for breast cancer. The data from several studies indicate that the use of breast MRI in patients newly diagnosed with breast cancer is still common and that a high degree of clinical uncertainty exists among surgeons as to its best use. As technical supports of breast MR imaging has been

improving with high-resolution and additional MR imaging, and focused usage of MRI for subpopulations of patients will benefit from preoperative breast MR imaging could improve the performance of MR imaging at the preoperative evaluation of breast cancer patients. In general, given the high number of false positives by MR imaging, however, it is always recommended that such suspicious sites be sampled first by percutaneous biopsy to avoid unnecessarily wide excision or mastectomy.

PN01-2

BREAST MRI, MINIMIZING POTENTIAL HARMS

Hyeong-Gon Moon

Dept. of Surgery, Seoul National Univ. Hospital, Korea

Breast MRI is the most accurate way of detecting breast cancer, determining the extent of cancer tissue, and finding occult tumors in axillary malignancies. Especially, MRI is particularly useful in patients who underwent neoadjuvant chemotherapy where the conventional imaging modalities often fail to yield accurate results. Additionally, MRI is a useful method of breast cancer screening in high-risk women.

However, it is still controversial in the use of breast MRI in primary breast cancer patients who are candidates for curative surgery. The well-known accuracy and sensitivity of breast MRI has brought up the enthusiasm that the use of breast MRI can reduce the rate of reoperation and the risk of future in-breast recurrences. Several studies have tested this hypothesis in breast cancer patients but have failed to produce a positive results. Furthermore, several retrospective studies have shown that the widespread use of MRI can result in increased incidence of mastectomies. In Korea, we are facing a unique situation in terms of the benefit of breast MRI since most of the surgeons routinely employ breast ultrasonography to determine the extent of breast cancer and to detect additional tumors before surgery. Since ultrasonography carries significantly higher sensitivity when compared to mammography alone, the potential benefit of breast MRI can be substantially lower in Korean breast cancer patients.

In this talk, I'll briefly review the current evidence of breast MRI in breast cancer patients in terms of potential advantages and drawbacks.

PN02-1

SURGICAL ISSUES FOR MANAGEMENT OF LOCAL-REGIONAL BREAST CANCER RECURRENCE

Hideko Yamauchi

Breast Center, St. Luke's International Hospital, Japan

It has been about three decades since breast conserving therapy (BCT) had been introduced in breast cancer treatment. We had been experienced ipsilateral breast cancer recurrence (IBTR). Salvage mastectomy had been considered the current standard of surgical procedure for ipsilateral breast cancer recurrence (IBTR).

Our goal for the treatment of IBTR is to achieve local control and survival benefit. Data from the Early Breast Cancer Clinical Trialists' Collaborative Group are explored the effect of local recurrence to overall survival. We learned local recurrence influenced survival in some extent. Therefore it is important to aim better local control for surgical management. Furthermore repeat conserving surgery may cause unacceptable cosmetic outcome. Especially our Asian population may have significant effect from volume loss.

On the other hand, there are risks of chest wall recurrence, even after salvage mastectomy. Rates of subsequent chest wall recurrence after salvage mastectomy for IBTR noted 2-32%. We have to consider mastectomy is not perfect to control local recurrence.

The impact from the advancement of systemic therapy and radiation therapy including partial breast irradiation may contribute to achieve better control. Technology of radiographic diagnosis has been improved recently. The introduction for MRI in the field of breast cancer management or ultrasound modality may play an important role to select appropriate patient for a good candidate to re-challenge breast conservation. Oncoplastic surgical techniques are introduced and we may able to obtain better cosmetic results after conserving surgery compared three decade ago.

There is a possibility to have some role for re-challenging breast conservation for IBTR in selected patients. We collected data from eight institutions to compare prognosis between salvage mastectomy with salvage breast-conserving for IBTR after BCT as a scientific research of Japanese Breast Cancer Society. A total of 271 consecutive patients who had histologically confirmed IBTR without distant metastases and underwent salvage surgery for the IBTR between 1989 and 2008 were included. We did not see any difference in distant disease-free survival between surgical procedures. We need to know which patient is good candidate for re-challenging breast conservation and how we can select. We will review data to compare salvage mastectomy with salvage breast-conserving and discuss surgical treatment for loco-regional recurrence in breast cancer.

<Co-Authors>
Atsushi Yoshida [1], Makoto Ishitobi [2]
[1] Breast Center, St. Luke's International Hospital, Japan
[2] Dept.of Breast and Endocrine Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan

PN02-2

RE-IRRADIATION AFTER IPSILATERAL BREAST RECURRENCE AFTER BCS

Kyubo Kim

Dept. of Radiation Oncology, Seoul National Univ. Hospital, Korea

Breast conserving therapy (BCT) comprising breast conserving surgery (BCS) and radiotherapy (RT) is the standard treatment for most of stage I-II breast cancer [1]. The incidence of ipsilateral breast tumor recurrence (IBTR) after BCT is on the order of 5-20% at 10-yr follow-up [2, 3]. In case of an IBTR after BCT, mastectomy is the most commonly used salvage treatment. The outcomes of repeat BCS alone have also been reported, but the number of such reports was very limited. In brief, the rate of 2nd IBTR is about 35% for these populations, which is similar to the rates of IBTR after BCS without RT for primary breast cancer[4-6]. Therefore, the feasibility of re-RT after repeat BCS has become the research interests of several investigators. Traditionally, interstitial brachytherapy has been selected as a method of re-RT. Partial breast irradiation (PBI) including interstitial brachytherapy limits radiation to only a portion of the breast, and can reduce radiation-induced toxicity. One retrospective study including 69 patients and three small prospective trials reported the local control rate of 77-100% in patients receiving interstitial brachytherapy after repeat BCS. The toxicity and cosmesis was acceptable, but the procedure was somewhat invasive. PBI using electron with conventional fractionation was also employed, and the reported local control rate was 77% [7] Recently, PBI using 3-dimensional conformal RT was successfully introduced to BCT for primary breast cancer [8]. As in the primary breast cancer, it can be applied to re-RT for IBTR after BCT. The ongoing Radiation Therapy Oncology Group phase II trial is evaluating the adverse events of repeat BCS and re-RT using 3-dimensional conformal RT in patients with IBTR after BCT.

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PN02-3

DO WE NEED SYSTEMIC TREATMENT IN PATIENTS WITH LOCOREGIONAL RECURRENCE?

Yee Soo Chae

Dept. of Medical Oncology, Kyungpook National Univ. Hospital, Korea

Isolated locoregional recurrence (ILRR) is associated with a worse prognosis as most patients with ILRR are believed to develop distant metastases despite aggressive local treatment. Although the role of systemic adjuvant treatment is well established in the management of primary breast cancer, we do have only limited evidence for the systemic treatment in patients with ILRR after complete resection or radiotherapy. For the hormonal treatment, tamoxifen after surgery demonstrated prolonged disease-free survival related with a reduced incidence of second locoregional recurrence in a phase III clinical trial. Meanwhile, there had been no prospective randomized trial of adjuvant chemotherapy for ILRR until the result of a recent international trial (CALOR trial). In this study, chemotherapy after local treatment was strongly associated with a better DFS (HR=0.59; 95% CI=0.35-0.99; p=0.046) and OS (HR=0.41; 95% CI=0.19-0.89; p=0.02). Based on the current evidences, adjuvant chemotherapy and hormonal treatment can be recommended for patients with completely resected ILRR. Furthermore, future studies are warranted to identify who can benefit from the systemic therapies or which regimen should be given.

PN03-1

UPFRONT SURGERY VS. SURGERY AFTER NEOADJUVANT CHEMOTHERAPY

Eun Sook Lee

Division of Convergence Technology, National Cancer Center, Korea

Neoadjuvant or preoperative chemotherapy has shown efficacy similar to adjuvant chemotherapy in operable breast cancer with the added benefits of improvement of surgical options and early determination of chemo-sensitivity. The main benefit of primary chemotherapy in operable disease is that it results in down staging of large tumors prior to surgery and it also appears to reduce the extent of local surgery required.

In a number of important randomized trials (National Surgical Adjuvant Breast and Bowel Project [NSABP] B-18, NSABP B-27, Mauriac et al., Scholl et al., European Organization for Research and Treatment of Cancer [EORTC] 10902, Petrov Institute, Powles et al.), patients with breast cancer were evaluated and chemotherapy was compared in the preoperative or the postoperative setting From these trials, the effectiveness of preoperative chemotherapy on operation method was also reported. The NSABP B-18 trial was the first study to compare postoperative with preoperative chemotherapy. The NSABP protocol B-18 reported that the size of primary breast tumors was clinically reduced in 80% of patients treated preoperatively and no tumor could be detected clinically in 36% of the patients. The trial resulted in a 7% higher rate of BCS compared with the postoperative treatment arm (60% vs. 67%, $p<0.01$) [3]. The European Cooperative Trial in operable breast cancer (ECTO) showed an increase in BCS from 34% in the postoperative treatment arm to up to 65% by preoperative chemotherapy ($p<0.001$). The EORTC 10902 trial also demonstrated an improvement in the BCS rate by preoperative chemotherapy: 21% (postoperative treatment arm) vs. 37% (preoperative treatment arm). Moreover, the EORTC 10902 trial showed that 23% underwent BCS among the patients who were planned for mastectomy in the preoperative chemotherapy group. Our study showed that the conversion rate to BCS was 38%. This result translates into a successful effect of preoperative chemotherapy in this study compared with other studies in Westernized countries. However, there are still controversies in how we could safely determine the tumor area and in high rate of loco-regional recurrence of BCS after chemotherapy.

The other issue will be the accuracy of the sentinel lymph node biopsy (SNB) and skipping axillary lymph node dissection (AXLD) when SNB is negative after chemotherapy who was positive for axillary metastasis in initial step. Reports on the efficacy of SNB after pre-operative chemotherapy have been inconsistent leading to suggestions that chemotherapy may interfere with the anatomy or physiology of the lymphatics and adversely affect its accuracy. In meta-analysis of SNB after pre-operative chemotherapy in patients with breast cancer, it shows that SNB is a reliable tool for planning treatment after pre-operative chemotherapy. But it shows the variability of this technique; the identification rate ranged from 72 to 100% and the sensitivity ranged from 67 to 100%. In our own prospective study of 284 patients whose axillary lymph node status was confirmed to be positive by 18F-FDG-PET or fine-needle aspiration cytology the SNB identification rate in chemotherapy-treated patients was 72.2% and the false negative rate was 11.1% These rates were markedly different in studies where pre-

operative chemotherapy was administered according to primary tumor size regardless of axillary node status. The current report in Lancet Oncology, Thorsten Kuehn and colleagues report findings of SENTINA, a prospective, multicentre cohort study of 1737 patients, all of whom received at least six cycles of anthracycline-based neoadjuvant chemotherapy. Sentinel-lymph-node biopsy done after neoadjuvant chemotherapy was less successful. Their findings suggest that sentinel-lymph-node biopsy should be done only once, after neoadjuvant chemotherapy. The study will be validated by long-term follow-up, with attention to patterns of local, regional, and distant recurrence.

Here, we will discuss upfront surgery vs. surgery after neoadjuvant chemotherapy for stage II/III breast cancer patients in terms of breast and axillary nodes.

PN03-2

ONCOLOGY ISSUE: ARE WE READY TO USE DIFFERENT STRATEGY ACCORDING TO INTRINSIC SUBTYPES?

Yeon Hee Park

Dept. of Hematology-Oncology, Samsung Medical Center, Korea

Neoadjuvant treatment of breast cancer enabled improved outcomes to facilitate surgery and to achieve pathologic response. Furthermore, it can accelerate new drug approval as “in vivo vehicle”. However, biological heterogeneity of these tumors requires better molecular characterization of the malignant tissue with consequent individualization in the selection of appropriate treatment strategies. pCR (pathologic complete response) is a meaningful short-term surrogate of outcome I more aggressive tumor (particularly HER2+ and triple negative tumors) and provide a strong rationale for testing new agents targeting highly proliferative tumors in the neoadjuvant setting using pCR as a primary end point. In contrast to this, the neoadjuvant setting also allows for evaluation of endocrine therapies in combination with newer targeted therapies in the appropriate patient populations (ER+ tumors).

Although current standard therapies provide substantial benefits for patients with a pCR at surgery, patients with residual disease are at substantial risk for disease recurrence, with the majority of patients with HER2+ or triple negative breast cancer who do not achieve pCR developing distant metastatic disease within the first three years after therapy. Therefore, efforts to improve pCR rates and develop alternative therapies for women with residual disease following standard therapy are clearly needed.

Insights into the heterogeneity and biology of breast cancer obtained through gene-sequencing and other technologies have identified a large number of potential targets in these tumors for newer, more selective investigational agents. The neoadjuvant setting provides an opportunity to accelerate evaluation of these agents and identify predictive biomarkers for response, as well as to gain insights into mechanisms of resistance. Other interventions, including immunotherapy and complementary approaches in the neoadjuvant setting, are also being used or are under consideration.

An alternative development approach would be to study new agents in patients with high-risk residual disease following standard treatment regimens. The NSABP, GBG, and other investigators are collaborating on a global trial (KATHERINE NCT 01772474) evaluating T-DM1 as an alternative to continuation of trastuzumab in women with residual disease following neoadjuvant chemotherapy combined with HER2 targeted therapy that includes trastuzumab. Patients with residual disease following NACT and trastuzumab have a three-year RFS of only 70%, so they are appropriate candidates for evaluating promising new therapeutic agents such as T-DM1. If successful this trial would establish a new approach for drug development.

Two innovative trials are in progress to address residual disease in patients with triple-negative breast cancer. The Hoosier Oncology Group is currently evaluating the benefit of cisplatin with or without a PARP inhibitor, rucaparib (Clovis) in women with triple negative or ER+/BRCA-mutant breast cancer who have residual disease in the breast after neoadjuvant chemotherapy with an anthracycline and/or

taxane-based regimen (NCT01074970). The primary end point of this trial is two-year DFS. The ABCDE trial (Adjuvant Bevacizumab, Metronomic Chemotherapy Diet and Exercise) being conducted within the Translational Breast Cancer Research Consortium (TBCRC) enrolls patients with triple negative or high-stage ER+ disease who have received anthracycline and/or taxane-containing neoadjuvant chemotherapy and have residual disease at surgery.

Not surprisingly, responses to neoadjuvant chemotherapy for patients with ER+ tumors are low and the outcome of ER+ tumors is not associated with pCR. Given these observations, the neoadjuvant setting is ideal for evaluating endocrine therapies in combination with newer targeted therapies in appropriate patient populations. ACOSOG conducted a follow-up randomized phase II neoadjuvant trial (Z1031) comparing the three approved aromatase inhibitors in postmenopausal women with ER-rich stage II to III breast cancers. They demonstrated an overall clinical response rate of 63% and that breast-conserving surgery could be performed in 50% of patients who presented with disease that would have required mastectomy at presentation. The ALTERNATE trial (ACOSOG Z11103) will be a phase III study comparing anastrozole vs. fulvestrant vs. the combination as neoadjuvant endocrine therapy in postmenopausal women with ER-rich stage II and III breast cancer. This innovative approach has established neoadjuvant endocrine therapy as a valid treatment and research option for ER-rich early breast cancer and will likely be further exploited in the future for combination endocrine/targeted therapy trials.

Taken together, it is time to adapt different therapeutic strategies for each intrinsic subtype in neoadjuvant setting. Obviously, the neoadjuvant setting provides several important opportunities for translational drug development. In addition, molecular and genetic profiling of residual disease after neoadjuvant therapy is an active avenue of investigation into potential targets of resistant disease.

In conclusion, the advances brought about by neoadjuvant therapy in both standard and investigational settings have ushered in a more personalized approach to breast cancer therapy that could result in improved survival.

PN03-3

SURGICAL ISSUE: CAN SLN BIOPSY GUIDE EXTENT OF LN DISSECTION AFTER NEOADJUVANT TREATMENT?

Joon Jeong

Dept. of Surgery, Gangnam Severance Hospital, Yonsei Univ., Korea

Use of sentinel-lymph-node biopsy as standard care for axillary staging in patients with clinically node-negative breast cancer is established by scientific literature covering all aspects of the procedure. Women with negative sentinel lymph nodes do not need axillary dissection because axillary local recurrence after the biopsy procedure is rare. Furthermore, axillary-lymph-node dissection offers no benefit over sentinel lymph node biopsy (SLNB) with respect to survival or morbidity.

However, the role of sentinel-lymph-node biopsy in patients receiving neoadjuvant chemotherapy (NAC) remains controversial. NAC is the standard of care for patients with locally advanced breast cancer. Growing evidence supports that NAC is reasonable alternative to adjuvant chemotherapy for those with large operable disease. Several randomized controlled trials have shown no differences in outcome between neoadjuvant and adjuvant chemotherapy. Achievement of pathologic complete response (pCR) correlates with excellent long-term outcome.

For those receiving NAC, feasibility and accuracy of SLNB is an urgent concern. Various studies including single institute trials, multi-center trial, and meta-analysis regarding this issue were reported. Recent studies, which collectively examined, concluded that SLNB after NAC is a reliable tool for planning treatment after NAC.[1] Currently, a National Cancer Institute conference recommended that SLNB could be performed after NAC in patients with clinically negative nodes at initial diagnosis.[2]

Recent studies focus on the patients with clinically node-positive cancer before NAC. About 40% of node-positive patients achieve a pathological complete response with current neoadjuvant chemotherapy protocols and might avoid axillary-lymph-node dissection. Several small studies suggest that SLNB after NAC is clinically feasible for those with positive node at presentation. However, most studies, provided by backup axillary-lymph-node dissection, are limited by small size, retrospective design, and wide variation in results.

Two large clinical trials to determine the accuracy of SLNB in the patients with clinically positive node is recently reported. An American College of Surgeons Oncology Group Z1071 clinical trial (ACOSOG Z1071) and SENTINA trial, the prospective German, multi-institutional trial, similarly suggest that technique matters for SLNB after NAC.[3, 4] The detection rate was higher, and the false-negative rate lower, with a combined dye-isotope technique than with isotope alone, and FNR was lower with the removal of more sentinel lymph nodes.

With a long-term follow-up, more attention to patterns of local, regional, and distant metastasis for those enrolled at these studies is needed. In patients receiving NAC, axillary failure rate could be the most significant outcome measure, not the FNR.

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PN04-1

CHALLENGES OF BREAST CANCER PREVENTION AND CONTROL

Hee-Soon Juon

Dept. of Health, Behavior&Society, Johns Hopkins Bloomberg School of Public Health, U.S.A.

Breast cancer is the most prevalent cancer in the world. More than 1.38 million women worldwide are diagnosed with breast cancer in 2008 (23% of all cancers). About 40% breast cancer cases are Asian women. The incidence of breast cancer in Asian countries was lower than in Western countries. In the past decade, breast cancer incidence rates in the U.S. have been decreased, while the morbidity and mortality related to breast cancer has been strikingly increased in Asia. By 2020, 70% of all breast cancer cases worldwide will be in developing countries. About 40% of all cancer mortality can be prevented which are linked to social and behavioral factors such as smoking, diet, alcohol use, sedentary life-style, and accidents.

The purpose of this session is to provide the challenges of breast cancer prevention and control in Asia. Moreover, these challenges will be addressed from the public health perspectives including low public awareness of breast cancer and breast cancer prevention, limited resources on breast health, late stage at diagnosis related to low breast cancer screening rates, barriers to breast cancer screening, and lack of comprehensive breast cancer program.

Comprehensive breast cancer requires continuum focusing on prevention, prediction, early detection, treatment, and survivorship. In countries with limited resources, prevention and early detection will play a pivotal role to increase survival rates and decrease cancer burdens for patients, family, and society. In the U.S., the five-year breast cancer survival rate is 83 percent. By contrast, Europe's rate is 69 percent and China's survival rate is 61 percent. This low survival rate is associated with low breast cancer screening. We need to reduce breast cancer disparities in Asia by increasing breast cancer awareness among Asian women in consideration of cultural differences of breast cancer such as the myths of breast cancer. Furthermore, we need to work on progress in the prevention, early detection, and treatment of breast cancer. We suggest that increasing our understanding of breast cancer prevention and control will require multidisciplinary approach to collaborate efforts among researchers, health professionals, breast cancer advocates, and policy makers.

PN04-2

CHALLENGES OF BREAST CANCER DIAGNOSIS AND TREATMENT IN 21ST CENTURY

Soonmyung Paik

Division of Pathology, National Surgical Adjuvant Breast and Bowel Project(NSABP) Foundation, Inc., U.S.A.

PN04-3

CHALLENGES AND POLICY IMPLICATIONS OF SUPPORTIVE CARE IN KOREA

Norma F. Kanarek

Dept. of Environmental Health Sciences, School of Public Health, Johns Hopkins Bloomberg, U.S.A.

There are many challenges in addressing best treatment and cancer prevention. Progress in these areas must go hand in hand with continuous learning from and about patients. Part of the prevention and treatment challenge is working with patients to effect the best change in breast cancer occurrence and outcomes.

Patients are multifaceted individuals and breasts are a significant part of being a woman. To meet these challenges, breast cancer patients and women at risk need knowledge, no nonsense advocacy, interventions, and policies that life affirming.

Knowledge Information for patients is essential to decision making and ultimate outcomes for women at risk. As soon as a cancer diagnosis is made, many physicians are engaged and the patient's families and friends network is activated. Becoming an "equity partner" in breast cancer care means that patient acquisition of information about and understanding of the nature of basic treatments in a negotiation, cancer care may be complex as evidenced by the potential web of physicians, and we will speak frankly with those around us.

No nonsense advocacy Breast cancer patients have good survival prospects, especially when detected early, so maximizing treatment completion is a goal. Patients should mobilize their personal networks to assist with deciding to get care, getting to care, and realizing emotional support. Medical center navigation where it exists may assist with mutable barriers to obtaining care such as transportation, child care, and so on. Today begins the era of individualized care when treatment options are tailored, many personal preferences can be met, and when participation in a research study is a viable treatment option.

Interventions Lessons from our decades long war on cancer have led to more sophisticated weapons that can be better aimed to fittingly treat the disease in this woman at this time. Medical centers have an opportunity to serve women from childbearing to old age and breast cancer is part of that continuum. Anticipation and treatment of iatrogenic problems is necessary. And most importantly breast care physicians have a prevention tool box. What can be done right now to reduce breast cancer risk?
Policy As medical and public health systems, our policies can shape and foster best outcomes. One stop shops for mammography, multidisciplinary clinics for diagnosis and treatment recommendation, institution of best practices among all populations, and health in all policies, each convey protection from high incidence, unnecessary care, and poor access. Engagement of Korea CDC and the use of their population health surveys will allow identification of populations at risk.

In summary, the many challenges of caring for patients with breast cancer may be addressed with knowledge, no nonsense advocacy, interventions and policy. A reordering of these important aspects of caring for women at risk of and with breast cancer will translate to PINK.

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IG01-1

IS THE AGE OF THE PATIENTS A CONTRAINDICATING FACTOR TO BREAST CONSERVATION?

Toru Watanabe

Dept. of Medical Oncology, Hamamatsu Oncology Center, Japan

The risk of local or regional recurrence of breast cancer is governed by several factors. These include the anatomical extent and the biological aggressiveness of the disease as reflected in its intrinsic subtype. Surgical management has been believed to reduce this risk. In the St. Gallen Consensus Panel Session in 2013, the Panel found that very young age(less that 35 year old) is one of the relative but not absolute contraindications to breast-conserving surgery. However, there is no robust evidence to show that a more extensive surgery such as mastectomy will overcome this risk. Recent evidence supports that effective systemic therapy may decrease the risk of not only distant metastases but also loco-regional recurrence, by irradiating micro metastases. Important considerations related to the age of the patients at the time of planning the local therapy include the intrinsic subtype of breast cancer, family history and mutations of the BRCA1 or BRCA2 genes. Another important consideration is the fertility of the patients who wish to become pregnant after treatment of breast cancer.

IG01-2

PREGNANCY ASSOCIATED BREAST CANCER

Hyun Jo Youn*

Dept. of Surgery, Chonbuk National Univ. Hospital, Korea

Pregnancy associated breast cancer (PABC) is commonly defined as breast cancer diagnosed during pregnancy or in the first postpartum year. The incidence of PABC is 1/3000 pregnancies, and it may account for up to 6.25% of all breast cancers diagnosed in fertile women under 45 years. Given the apparent rising incidence of PABC, perhaps due to trends in delaying pregnancy, a greater understanding of the histological features, treatment options, and maternal and fetal outcomes is critical.
As the majority of PABC occur in women<40 years, BRCA mutations are over-represented in this group. Therefore, PABC patients should be offered genetic testing. There is an increased incidence of ER-negative breast cancer during pregnancy, but this increase may be artificial, due to high circulating estrogen levels competing with the binding assay.

Diagnosis of PABC is often delayed. This delay is partly because of a lack of suspicion of the breast cancer in young age and difficulties in establishing the diagnosis. Physiological changes in pregnancy and lactation, due to increased hormone levels, result in an increase in breast volume and firmness. These changes make clinical and radiological detection and evaluation of breast masses difficult. Breast ultrasound is of high sensitivity and specificity in diagnosing PABC and is, therefore, considered the standard method for the evaluation of a palpable breast mass. Following diagnosis, staging investigations should only be undertaken for clear clinical indications and even then may be modified in terms of the choice of investigative method in the light of the pregnancy.

Treatment of PABC requires a multidisciplinary approach and careful consideration of the patient's stage of disease, the gestational age, and the preferences of the patient and her family. Surgery is the first line of treatment for PABC, with modified radical mastectomy being the treatment of choice for operable disease. In patients who are not pregnant, there have been multiple studies showing similar survival in women who undergo breast conserving surgery plus radiation when compared with mastectomy. Radiation therapy is, in general, contraindicated in pregnancy, due to an increased risk of fetal malformations and associated delays in neurocognitive development. During pregnancy, several physiologic changes alter the pharmacokinetics of chemotherapeutic agents, increasing or decreasing both the potential efficacy and the risk of toxicity. Chemotherapy is contraindicated in the first trimester of pregnancy because of the risks of teratogenicity during organogenesis. And endocrine therapy is not recommended during pregnancy. The timing of delivery should be as near the expected date as possible. There is no evidence that termination of pregnancy will improve the prognosis in PABC. Lactation from the treated breast is not contraindicated.

Although most studies have indicated equal prognosis of PABC when matched for age and stage, a recent article showed poorer survival in those with PABC. It is unclear whether this is due to less aggressive therapy secondary to concern for fetal effects, a later stage at diagnosis due to diagnostic

delay or accelerated growth owing to increased vascularity, hormonal exposure, or suppression of the immune system during pregnancy. Fewer than 10% of women affected with PABC have become pregnant after treatment, and little is known about what effects a future pregnancy will have on the risks of breast cancer relapse.

Randomized controlled trials are unlikely to succeed because of the rare incidence of PABC. Continued prospective data collection and case series publication may improve comfort with using contemporary treatment to care for women in the difficult situation of PABC. When making treatment decisions for these patients, attention to multidisciplinary team management is necessary to appropriately balance perinatal care of mother and infant. Further data collection and investigation will improve understanding of and treatment paradigms for PABC.

IG01-3

FERTILITY PRESERVATION FOR EARLY BREAST CANCER : MEDICAL ONCOLOGIST'S PERSPECTIVES

Ann H. Partridge

Dept. of Medical Oncology, Dana-Farber Cancer Institute, U.S.A.

When young women are diagnosed with breast cancer, they face not only the usual fears and concerns of a potentially life-threatening cancer and the need for treatment that can be quite toxic and disfiguring, but they also face unique concerns such as risk of infertility from treatment. For some young women, this issue is of paramount importance and fertility concerns may impact on treatment decisions for up to 30% of young women with early stage breast cancer. Attention to fertility early after diagnosis, when treatment decisions are being made, is thus extremely important. Thoughtful consideration of the risks of future infertility as well as options for fertility preservation with women who are interested and at risk is necessary. The standard, most widely available option for fertility preservation is in vitro fertilization and embryo cryopreservation prior to therapy. Another option is oocyte cryopreservation, as success rates have improved over the years using this technology. Use of ovarian suppression through treatment and cryopreservation of ovaries or ovarian tissue, particularly important for children and women who don't have the time to go through other methods or are concerned about risks of ovarian stimulation, remain experimental options. Each of the options has potential risks and benefits that need to be considered. Women need to be supported to make the best decisions for themselves and their loved ones in this setting given their preferences, available options and psychosocial support, particularly for women who may not be able to have children in the future should be provided.

IG01-4

CULTURALLY-SENSITIVE HEALTH PROMOTION PROGRAM ON BREAST CANCER FOR ETHNIC MINORITY WOMEN

Carmen Wing Han Chan

The Nethersole School of Nursing, The Chinese Univ. of Hong Kong, Hong Kong

Like many world-class cities, Hong Kong is a multi-ethnic society. The ethnic minority population keeps growing since last decade, increases from 343,950 in 2001 to 451,183 in 2011. About 72.6% of them are South Asians. Certain barriers exist leading to less access or participation in cancer preventive measures in this population, such as lack of health insurance coverage, traditional custom, values and beliefs, wrong perception of preventive measures, physician's attitude towards minorities, language barrier, logistic and financial constraints, unfamiliarity with local healthcare system, least knowledge of symptoms, risk factors and tests, uncomfortable in taking the test, and without physician recommendation.

Ethnic minority women are comparatively less educated and most of them are housewives. They are inaccessible to healthcare services with poor knowledge of cancer risk factors, warning signs, detection methods and treatments. Traditional custom and cultural beliefs are major barriers, for example, Nepalese women are subordinate to and obedient to their husband at home, the taboo of touching oneself in breast self-examination, and feeling embarrassed about the discussion or examination of intimate body parts by male physician.

Thus, we have conducted a service project tailored for this ethnic minority women group (Indians, Nepalese, Pakistanis) to provide them with culturally-sensitive information related to breast cancer and currently available preventive measures. The project consists of three parts: 1. Health talk, 2. Practical demonstration, 3. Leaflets. The project also helps to strengthen the mutual help network among South Asian women.

Promotional strategies of the project included posters to be displayed in the collaborated ethnic minority support centers. Training workshops was organized to voluntary nursing students or South Asian women ambassadors. The contents of the proposed service project and skills in delivering health education materials were taught in the workshop. Ethnic minority translator(s) was also invited to join the training workshops.

Fifty three service recipients were recruited via the collaborated support centers. The number of nursing students involved was21. Pre-test post-test evaluations using a short questionnaire were conducted in order to assess their knowledge, attitude and perception about cancer. The program lasted for about two hours. In which, 40minutes was allocated to health talk that was conducted in English and interpreted by a translator, 15-30 minutes for question and answer section, and the remaining 50 minutes for practical demonstration of breast self-examination. Besides, leaflets with breast cancer and screening services information, in English, Nepali or Urdu were distributed to service recipients.

After the completion of program, a debriefing session was conducted with nursing students, South Asian women ambassadors and translators.

Preliminary findings will be shown in the presentation. In summary, dispelling the myths and misconceptions of breast cancer helps to increase awareness of breast cancer and available preventive services. As South Asian women ambassadors were involved in the program, they helped in building up the mutual help network among the South Asian society and empowered these women to make own health decision. With the provision of tailored health promotion strategies for South Asian women in Hong Kong community, their health preventive needs are met and their sense of belonging to Hong Kong is increased.

<Co-Authors>
Chan D.N.S., So W.K.W., Chen J.M.T., Sit J.W.H.,
The Nethersole School of Nursing, The Chinese University of Hong Kong, Hong Kong SAR, China

IG01-5

PRESERVATION OF OVARIAN FUNCTION IN YOUNG AGE BREAST CANCER

DooSeok Choi

Dept. of Obstetrics & Gynecology, Samsung Medical Center, Korea

Breast cancer is one of the most common malignancies in Korea as well as in other countries. As many women with breast cancer are diagnosed in reproductive ages, and survival rates have been improved dramatically over the past decades. Therefore, fertility issue should be addressed with higher priority in the aspect of quality of life.

Concerns have been raised regarding gonadal toxicity by commonly used chemotherapeutic regimen including cyclophosphamide which can lead to ovarian damage or even premature ovarian failure. To preserve fertility potential, several approaches have been attempted in young breast cancer patients who must undergo chemotherapy, such as cryopreservation of oocytes or embryos, and even ovarian tissue. In addition, to prevent or reduce chemotherapy-induced gonadal toxicity, ovarian suppression by gonadotropin-releasing hormone (GnRH) analogue also has been used.

In this presentation, the options for the preservation of ovarian function in young age breast cancer patients will be discussed.

IG01-6

PSYCHIATRIC CONSULTATION AND PSYCHOSOCIAL INTERVENTION FOR YOUNG AGE BREAST CANCER

Seong-Jin Cho

Dept. of Psychiatry and Psycho-oncology, Korea Cancer Center Hospital, Korea

Younger women with breast cancer undergo more aggressive treatment and face a variety of unique treatment and psychosocial issues. All of these factors contribute to the risk of greater psychosocial distress in these younger women. A breast cancer diagnosis can be devastating, irrespective of the age of the women at diagnosis. However, there are a number of issues that may be particularly pertinent to younger women who are diagnosed with breast cancer. Younger breast cancer survivors may be in need of interventions that specifically target these issues. In relation to this, we should understand the threat that breast cancer pose to attaining age appropriate development goals (e.g., marriage, pregnancy, child bearing, career). Younger patients diagnosed with breast cancer will experience a range of practical, psychological and social challenges as a result of their diagnosis and the adverse effects of treatment. Increasing attention to their unique issues may improve care and outcomes for this vulnerable population. Early delivery of efficacious psychosocial interventions may potentially improve mental health, treatment-related health behaviors and biological outcomes in breast cancer.

We have served as psychiatric consultation many younger patients with breast cancer. Although only a small portion of breast cancer occurs in women younger than 40 years of age, a disproportionately large number of these women seek psychiatric consultation. Among the conditions treated were anxiety disorders, cognitive disorders(chemo-brain, delirium, and dementia), mood disorders, suicidal emergency, sleep disorders, physical symptoms(fatigue, nausea, vomiting, cardiovascular and respiratory symptoms), personality disorders, refusal of treatment, unrelieved pain, side effects of cancer treatment, somatoform autonomic dysfunction, unexplained psychosomatic problems. Young women who receive adjuvant chemotherapy and experience drug-induced menopause are at a greater risk for negative changes in sexuality and poorer sexual functioning outcomes. In addition, breast cancer in younger women is often temporally related to a recent pregnancy or may occur during pregnancy, and thus, these women often have small children to care for at the same time that they must deal with a life-threatening disease. In relation to this, issues especially specific to younger breast cancer patients are sexual side effects of treatments, menopausal symptoms, fertility and child rearing, self and body image, post-mastectomy neuropathy, genetic risk, education and career, appearance and beauty, relationships, and prophylactic mastectomy. The additional unique reasons for consultation were information management, communication issues, end-of-life issues, bio-ethical issues, family therapy, complementary medicine, decision-making, bereavement, and issues specific to the cancer site.

The interventions for women with breast cancer include psychopharmacotherapy, psychotherapy, specialized program and complementary treatments. Patients could be referred to other specialized services, including social work, hospice and palliative care, which were aimed to improve the quality of

life and bio-psycho-social distress of them. The psychosocial programs and hospice care have been incorporated into cancer care over ten years in Korea Cancer Center Hospital; self-help group, art therapy and specific psychosocial group programs. As a result, patients as well as family members have shown great levels of satisfaction. Communication is central to cancer care delivery. Health professionals involved in the management of younger women with breast cancer should more fully understand the experience of women with psychosocial distress. The aim of this presentation is to bring our hands-on experiences and contribute by bringing Korean clinical data that help clinicians and researchers at the GBCC 2013 facilitate the exchange of their own experiences from different cultural backgrounds and national perspectives.

IG02-1

WHERE ARE WE IN ASIA, TWO DECADES AFTER THE DISCOVERY OF BRCA1 AND BRCA2

Sung-Won Kim

Dept. of Surgery, College of Medicine, Seoul National Univ. Bundang Hospital, Korea

Genetic predisposition is an important cause for developing breast cancer and it account for 5-10% of all breast cancer patients. Several high- and intermediate-penetrance genes associated breast cancers have been identified, which include BRCA1, BRCA2, PTEN, TP53, STK11, CHEK2, ATM, BRIP1 and PALB2. BRCA1 and BRCA2 mutations account for almost half of hereditary breast cancer.

The first reports of BRCA1 and BRCA2 mutations were by Miki et al. (1994) and Wooster et al. (1995). During the past 20 years after discovery of BRCA mutation, a lot of biologic, epidemiologic and clinical researches for hereditary breast cancer have been performed. The function of BRCA1 and BRCA2 was discovered and those are tumor suppressor genes which repair double-stand DNA breaks by homologous recombination. Various prevalence studies showed that BRCA1/2 mutations rates are 3-8% of all breast cancer patients and 15-20% of breast cancer patients with family history of breast cancer. Several factors also increase the risk of carrying a BRCA mutation, which include early-onset breast cancer, bilateral breast cancer, history of both breast and ovarian cancer, male breast cancer, and triple-negative breast cancer (ER-negative, PR-negative, and HER2-negative). Founder mutations of BRCA1 or BRCA2 have been identified in Iceland, Greenland, Cyprus, Bahamas, Dutch, French-Canadians, Poland, and Russia. 185delAG and 5382insC in BRCA1 and 6174delT in BRCA2 are well known founder mutations in Ashkenazi Jewish, which account for most of BRCA mutations (>90%) in this population. Finding founder mutations is important because it can make the genetic test simple and inexpensive. To select appropriate candidates for BRCA genetic testing, several BRCA risk prediction models based on Caucasians data were developed including Myriad II, BRCAPRO, BOADICEA, Manchester, and LAMBDA. In a meta-analysis, the risks of developing breast and ovarian cancers among BRCA1/2 mutation carriers by the age of 70 years were 57% (95% confidence interval [CI], 47-66%) and 40% (95% CI, 35-46%) for BRCA1 mutation carriers and 49% (95% CI, 40-57%) and 18% (95% CI, 13-23%) for BRCA2 mutation carriers, respectively. Individuals with BRCA mutations receive personalized management strategies including intensive surveillance and prophylactic surgeries according to their cancer risks. Numerous retrospective studies have been performed to evaluate the efficacy of prophylactic surgeries. Prophylactic mastectomy reduces the risk of breast cancer by 90%, and prophylactic oophorectomy reduces the risk of ovarian and breast cancers by 95% and 50%, respectively. In vivo and in vitro studies for treatment of BRCA-related cancer showed that BRCA1-related breast cancers would be sensitive to DNA-breaking agents (mitomycin C and cis-platinum). And also, poly (ADP-ribose) polymerase inhibitors (PARP inhibitors) have shown effectiveness in treating BRCA-related breast cancers. Clinical guidelines for management of hereditary breast and ovarian cancer were well established based on these evidences. However, most of studies have been performed in Western countries with high incidence of breast cancer relatively.

Breast cancer incidence is gradually increasing in Asian countries due to change in lifestyle and reproductive factors, and breast cancer is the most common cancer among Asian women. Early-onset breast cancer in Asia is relatively high and hereditary breast cancer occurs disproportionately in young women, therefore, genetic predisposition, BRCA1 and BRCA2, is expected to account for a greater proportion of all breast cancer in Asia. Over the past decade, BRCA genetic testing has been increasing and a variety studies have been performed to identify the characteristics of hereditary breast cancer in Asia. Furthermore, for collaborative studies, the Asian BRCA (ABRCA) Consortium was established in 2011, which initially consisted of Korea, Malaysia, Hong Kong, Japan, China, Indonesia, and Singapore. The aims of the ABRCA Consortium are to share knowledge about HBOC among Asian countries, improve the quality of care for patients with HBOC in Asia, and undertake collaborative studies on HBOC in Asia. To date, the annual meeting has been held in 2 rounds, in Malaysia (2012) and Hong Kong (2013), and includes participants from India, the Philippines, and Vietnam. The ABRCA working groups are conducting collaborative studies to review the BRCA mutation spectrum and founder mutations in Asia and evaluate the status of genetic counseling and genetic testing for HBOC in Asian countries. The working groups are also planning to study the lifestyle modifiers of breast cancer and estimate the penetrance of BRCA mutations in Asian populations. Through this scientific program “Asian Hereditary Breast Cancer” in GBCC, we will review the current status of researches for hereditary breast cancer in Asia and collaborative studies of ABRCA Consortium.

IG02-2

SYSTEMIC REVIEW OF BRCA MUTATION AND VARIANTS OF UNKNOWN SIGNIFICANCE IN ASIA

Ava Kwong

Breast Surgery Division, Queen Mary and Tung Wah Hospital; The Univ. of Hong Kong; The Hong Kong Hereditary Breast Cancer Family Registry, Hong Kong

The prevalence of breast cancer in Asians is lower than in Caucasians. However, the age of onset has been noticeably younger in Asian population. Approximately 5-10% of breast cancers patients are due to inherited genetic predisposition caused by germline mutations of which majority are due to mutations of BRCA1 and BRCA2 genes. It has been reported that the spectrum of BRCA mutations varies depending on the geographical origin, populations or ethnic groups and there is a high likelihood of finding novel mutations in cohorts where genetic testing is still less accessible. Also it has also been suggested that although the prevalence of BRCA mutations are likely to be similar to Caucasians, BRCA2 mutations are more common in Asian cohorts. The ABRCA (Asia BRCA Consortium) collected data available from 9 Asian countries (China, Hong Kong, Japan, Korea, Malaysia, Philippines, Singapore and Vietnam and Bangladesh) and also data in Asians residing in United States and Canada of participating centers. Literature review was performed to include reported BRCA mutations in Asians where available in order to present the updated mutation spectrum of BRCA mutations in breast cancer patients in Asians. Prevalence of BRCA mutations in different countries was compared This review divulge a unique spectrum of BRCA mutations among Asian population, implicating the importance of genetic testing for BRCA mutation in high-risk patients with breast cancer.

IG02-3

RISK ASSESSMENT AND MODIFIERS OF THE RISKS OF BREAST CANCER AND BRCA MUTATION IN ASIA

Sue K. Park

Dept. of Preventive Medicine, College of Medicine, Seoul National Univ., Korea

Given different age-adjusted incidence and BRCA 1 and 2 mutation prevalence for breast cancer in Asian countries compared to those in western countries, there is a need for developing a risk assessment model and defining risk modifiers for estimating the risk of BRCA mutation and breast cancer development from Asian populations. Using a hereditary breast cancer study (KOHBRA) and a sporadic breast cancer study (SeBCS) in Korea, major risk factors for sporadic and hereditary breast cancer and the risk factors in relation to BRCA mutation were selected to establish three risk assessment models for breast cancer: 1) sporadic breast cancer risk assessment model (Model 1), 2) hereditary breast cancer risk assessment model (Model 2), and 3) BRCA mutation risk assessment model (Model 3). We validated these models by the expected/observed rates and the area under curve (AUC) using the Korean cohort participants such as Korean Multicenter Cancer Cohort [KMCC] and National Cancer Center [NCC] cohort, and the other source of hereditary breast cancer study from Asan Medical Center. In model 1, the C-statistic was 0.66; in model 2, the C-statistic was 0.60 for BRCA1 and 0.71 for BRCA2; and in model 3, the C-statistic was 0.76 for familial breast cancer and 0.62 for non-familial breast cancer. All models were validated in the other Korean population. Applying the western subjects based models directly to the Korean population for risk prediction may not be appropriate because a different pattern of incidence, prevalence of risk factors, and BRCA mutation prevalence and penetrance exists between Western and Asian countries including Korea. Due to difference in incidence, prevalence of risk factors, and BRCA mutation prevalence and penetrance among different populations, existing prediction models may not be directly applied to Asian women. There is an urgent need to develop a breast cancer prediction model to assess individual risks for developing breast cancer in Asian women, and to provide evidence-based guidelines for primary prevention and early detection to the public.

IG02-4

STATUS OF GENETIC COUNSELING AND GENETIC TESTING IN ASIAN COUNTRIES

Philip Iau

Dept of. Breast Cancer Services, National Univ. Hospital, Singapore

The discovery of BRCA mutations was followed by a rapid elucidation of clinical penetrance, histological and prognostic effects and interaction with other breast cancer predisposition genes. Transfer of this new knowledge of laboratory bench to clinical bedside has been relatively rapid, with large consortia and patient demand driving the development of widely accepted indications for screening and clinical intervention. BRCA mutation testing has now become part of standard investigations for suspected hereditary and early onset cancers in developed countries in the West.

In Asian countries the uptake of BRCA testing among healthcare agencies, physicians and at risk individuals has been as varied as the contrasts in cultural practices and healthcare demands across the continent. Prevalence analysis has generally shown similar levels as most western series, with exceptions in groups with founder mutations. Fewer countries have carried out penetrance effects across different races, an effort that is likely to require large numbers of multiple - cancer families. For the present most genetic counselors in asia have used risk models based on western datasets. This appears to apply to genetic testing carried within centres catering to patients with hereditary cancer syndromes as well as those where gene testing has been carried out based on histological subtypes.
Consistent with the lower uptake of genetic testing among Asian minorities in western countries is the proportion of at risk who agree to undergo mutation screening in Asia. This is also seen in the lower proportion of Asian women who share genetic information with the rest of their family members who may be at risk. The role of ethnic practices and beliefs in the choice for gene testing and preventive surgery is understudied.

Asian countries that have removed or reduced the common barriers to genetic uptake - the cost of the gene test and the potential of insurance discrimination - have seen a dramatically higher rate of genetic testing among those at risk. This illustrates the importance of the work of legislation and advocacy in partnership with molecular biologists and clinics if the potential of BRCA testing is maximized among Asian families.

IG02-5

EARLY DIAGNOSIS AND RISK REDUCTION STRATEGY IN BRCA CARRIERS

Seigo Nakamura

Division of Breast Surgical Oncology, Dept. of Surgery, Showa Univ., Japan

Background : Breast cancer is the most common female cancer in worldwide. Previously, the lifetime breast cancer risk among Asian countries was markedly lower than in the U.S. or Europe. However, the incidence has been rapidly increasing due to the westernized lifestyle mainly affected by dietary habit. The peak age of breast cancer incidence is between late 40s and early 50s among Asian woman which is 10-15years lower than in the U.S or Europe. Moreover, the size of the breast in Asian woman is modest and dense which is not suitable for mammography screening. The peak age of breast cancer incidence among BRCA1/2 carriers is 10-15years younger than in non-affected population. Therefore, we should pay much more attention to the screening method and other strategies for affected carriers. In this presentation, recent strategy for early diagnosis and risk reduction in BRCA carriers are suggested especially from the stand point of Asian population

Materials and Methods : BRCA 1 and 2 (BRCA1/2) data had been collected from 8 institutions in Japan on 320 individuals with a strong family history of breast cancer, according to the NCCN guidelines, by the end of March, 2012.

Results : Among 260 proband cases, 46 (17.7%) were positive for BRCA1 and 35 (13.5%) were BRCA2 positive. Therefore, the total pathological mutation rate was 30.7%. Pathology data after breast surgery were obtained from 35 cases of BRCA1 mutation, 22 (62.9%) of which were triple negative (TN) and 10 (29.4%) were Luminal type. On the other hand, 24 cases (85.7%) of BRCA2 mutations were Luminal type. 75% of BRCA1 cancers occurred under 50 and 35% were under 40, especially the incidence on 20s were mostly due to BRCA1 mutation.55 cases decided operation method after receiving the result of BRCA 1/2 testing. If the BRCA1/2 were positive, 87.5% of them preferred mastectomy followed by reconstruction instead of breast conserving surgery, on the contrary, 71.8% of non-affected cases selected BCS. No one desired contralateral prophylactic mastectomy in our series.

Discussion : From NCCN guideline, the screening program is recommended from age 25 with breast Gd enhanced MRI. MRI has higher sensitivity than conventional MMG or US, however, it is expensive and time consuming method. And higher false positivity has been often argued. The new technologies such as tomosynthesis in MMG, contrast-enhanced spectral MMG,and elastography in US should be validated whether it is the same capability as Gd enhanced MRI or not. PET mammography (PEM) followed by conventional PET scan is another promising method because it can evaluate pancreas, ovary, and other organs simultaneously. Those methods should be evaluated among ABRCA whether they are suitable for Asian woman or not.

Majority of BRCA1 positive breast cancer is TN which has the characteristics of expansive growth with pushing boarders. The growth rate is usually rapid and sometimes pointed out as interval cancer. Therefore, the personalized approach including intrinsic subtype should be taken into account.
Bilateral salpingo-oophrectomy has shown survival advantage for ovarian cancer among BRCA1/2 positive cases. Because there is not a reliable screening method .On the contrary, the survival advantage of prophylactic mastectomy among non-affected women has not been confirmed yet because there are several screening methods. Moreover, the issue of prophylactic contralateral mastectomy is controversial. The large scaled trials of tamoxifen or AI prevention have been conducted among high risk population in western world. They were based on the risk models such as Gail model or Claus model. Chemoprevention should also be evaluated among Asian population because there is huge difference between western and Asian women from the aspect of breast cancer risks.
Each prevention method has several advantages and disadvantages. And they are changeable according to age, social or emotional circumstances of individuals. Team approach including genetic counseling in timely manner will become much more important than ever.

Conclusion : HBOC may have nearly the same prevalence in Japan as in the U.S. or Europe.
Therefore, the same kind of screening strategy and risk reduction procedures should be taken into consideration for mutation carriers. However, modification of the strategies should be desired from the aspect of the characteristics of Asian women and health economics. Therefore, the activity of ABRCA will also be inevitable in this aspect. The configuration conducting clinical trials among ABRCA should be also discussed in the future.

IG02-6

OUTCOMES FOR ASIAN BRCA CARRIERS

Rajiv Sarin

Dept. of Radiation Oncology & Cancer Genetics, Tata Memorial Hospital & ACTREC; Cancer Genetics Lab (Sarin Lab), CRI, ACTREC, Tata Memorial Centre, India

Pathogenic or deleterious Germline mutations in BRCA1/2 genes confer a very high life-time risk of developing breast and or ovarian cancers. In addition, these cancers could differ from sporadic cancers in biological and clinic-pathological features and sensitivity to certain drugs like platinum agents and PARP inhibitors. Data from large Caucasian cohorts of BRCA1/2 mutation carriers over the last two decades has provided reliable estimates of penetrance; tumour phenotype (histological grade and triple negative status); therapeutic response to specific agents; clinical outcomes (local and distant disease free and overall survival); and toxicity in the BRCA carriers. However due to the much smaller and immature cohort of Asian BRCA1/2 carriers, which is further divided into even smaller cohorts of different countries and ethnicities within Asia, there is very little information in the literature and databases regarding the penetrance and clinical outcome of BRCA mutations in Asians.

In a cohort of 151 Indian BRCA1 and BRCA2 gene mutation carriers, we estimate that the penetrance of specific truncating mutations such as 185delAG and others is same as reported in the Jewish or Caucasian population i.e. 70-80% for breast cancer and 25-30% for ovarian cancers by age 80 years. There are very few pathogenic missense mutations in our cohort to reliably ascertain their penetrance. The cancer spectrum in cancer affected Indian BRCA1/2 mutation carriers is also similar with approximately 65% having unilateral or bilateral breast cancer, 20% having ovarian cancer and 15% having breast and ovarian cancers. Almost all the breast tumours in carriers of truncating mutations in BRCA1 gene were IDC grade III and triple negative (ER, PR and HER2neu). Unfortunately, most women in our cohort presented in late stages and experienced a poor clinical outcome. Of the 84 women with breast and or ovarian cancer and a confirmed 185delAG BRCA1 mutation in them or their relatives, 47(56%) died of their cancer at a mean interval of 30 months from cancer diagnosis and at a mean age of 49 years. With several rounds of pre and post-test counselling, there is increasing trend of adherence to surveillance and preventive surgery in Indian BRCA mutation carriers. Similar figures are yet to be reported from most Asian countries. In our cohort of 53 Indian BRCA1 Mutation Carriers who were counselled for risk reducing salpingo-oopherectomy (RRSO), 70% have undergone the procedure or are in the process of going through it. While the benefits of RRSO are emphasized in our practice and has very high uptake rates similar to the Western cohorts, bilateral prophylactic mastectomy is a procedure that we discuss but do not emphasize and is performed occasionally in our centre.

<Co-Authors>
P. Kowtal [2], A. Maheshwari [3], V. Parmar [3], N. Bhatnagar [1], J. Patel [2], G. Pandit [1], S. Abbas [2], V. Kembhavi [1]

[1.] Cancer Genetics Clinic, Tata Memorial Hospital & ACTREC, Mumbai

[2.] Cancer Genetics Lab (Sarin Lab), CRI, ACTREC, Tata Memorial Centre, Navi Mumbai

[3]. Surgical Oncology, Tata Memorial Hospital, Mumbai

IG02-7

BEYOND BRCA MUTATION IN HEREDITARY BREAST CANCER

Soo-Hwang Teo

Breast Cancer Research Unit, Cancer Reaserch Initiatives Foundation;
Univ. Malaya Medical Centre, Malaysia

It is estimated that BRCA1 and BRCA2 account for approximately 25% of excess familial risk to breast cancer. In my talk, I will review our molecular understanding of the other genes that contribute to hereditary breast cancer, summarise what we current know about the risks associated with each gene and provide an update of what we currently know about the relevance of these genes to the Asian population. This includes rare high penetrance genes such as TP53 and PTEN, and moderate penetrance genes including ATM, CHEK2 and PALB2. Finally, I will briefly provide an update on our current understanding of other genes and genetic loci identified through genome wide association studies and discuss whether these SNP based testing are ready for clinical practice.

GBCC2013

Education

ED01-1

GENOME-WIDE PROFILING OF BREAST CANCER: HISTORY AND LESSONS FROM STUDIES BEFORE NGS ERA

Wonshik Han

Dept. of Surgery, Seoul National Univ. Hospital, Korea

Microarray-based gene expression profiling analysis has undoubtedly had a dramatic impact on our understanding of breast cancer biology by bringing the concept of the heterogeneity of breast cancer to the forefront of research and clinical practice. Data from microarray studies performed over the past decade have led to a change in the way breast cancer is perceived and highlighted the concept that breast cancer is a collection of different diseases that require distinct therapeutic approaches. Estrogen-receptor (ER)-positive and ER-negative breast cancers have been identified as distinct diseases at the transcriptomic level. Moreover, additional molecular subtypes may exist within these groups, and prognosis of patients with ER-positive disease is largely determined by the expression patterns of proliferation-related genes. Although the molecular subtypes have become part of the breast cancer lexicon for researchers, oncologists, surgeons, and pathologists, significant limitations exist with respect to number of molecular subtypes, definition of each subtype, and their prognostic and predictive value. The information provided by these subtypes in addition to that provided by ER, PR, HER2 and proliferation remains to be fully established.

First-generation prognostic gene signatures (MammaPrint, 76-gene signature, Genomic grade index, Oncotype DX) provide complementary information to that obtained from anatomical prognostic variables, such as tumor size and nodal status. Current first-generation prognostic signatures are clinically useful in patients with ER-positive disease, but of limited clinical value for ER-negative disease. These signatures rely heavily on the prognostic power of proliferation-related genes. While the prognostic information offered by the signatures in addition to that provided by semi-quantitative analysis of ER, PR, HER2, and Ki67 is clearly limited, these tests offer an important, albeit incremental technical advance in terms of reproducibility and quantitative assessment of markers. A number of these signatures have been developed on or converted into platforms applicable to routinely processed tumor samples, such as FFPE (e.g., qRT-PCR Oncotype DX). Accumulating Level I evidence for the prognostic utility of Oncotype DX has been obtained. Notably, however, the development of gene signatures to predict response to specific agents has been less successful, and there are no commercially available tests as yet.

The theoretical, experimental, and statistical knowledge acquired from microarray-based gene expression profiling studies should aid in the development of the next generation of genomic predictors. Furthermore, Next Generation Sequencing data combined with the results of microarray gene expression profiling studies undertaken in the past decade will provide a unique opportunity to develop hypothesis-driven predictors of survival and response to specific targeted agents.

ED01-2

INTRODUCTION OF NEXT GENERATION SEQUENCING AND ITS CLINICAL IMPLICATION

Se-Hoon Lee

Dept. of Internal Medicine, Seoul National Univ. Hospital, Korea

Cancer genome data is increasing too rapidly. Many papers of cancer genome are being published and cancer genome data, accumulated in the TCGA (The Cancer Genome Atlas), is increasing explosively since the first human cancer genome data of small cell lung cancer and melanoma were published in 2010.

The interest in cancer genome is moving from the level of science to the clinical application, with the speedy drop-down of the cost of next-generation sequencing (NGS) technology.

Cancer genome analysis has explored many important issues of cancer genetics and biology, including chromothripsis and tumor heterogeneity. In addition, integrative genome analysis has characterized some subtypes of cancers, such as breast cancer and medulloblastoma in detail.

There are some hurdles to clinical application of cancer genome data. These are cost, time, ethical issue, accessibility of analysis platform and et al. But the most important issue is the influence of personalized cancer genome result on treatment strategy. Classical anticancer treatment paradigm was based on site and histology of cancer. Although some target agents such as imatinib, gefitinib and trastuzumab (Herceptin®) are chosen based on molecular profile of the cancer, the most of clinical decision is still based on site and histology of cancer. Another important obstacle is tumor heterogeneity. Two representatives of successful target agents, imatinib and gefitinib, target universal molecular changes in specific cancers. Bcr/abl translocation for chronic myelogenous leukemia and EGFR mutation for never-smoker lung adenocarcinoma are found almost all parts of cancers. But all the genetic alterations aren't widespread through regions of individual tumor.

Along with the advent of the concept of "precision oncology", direct connection between personalized cancer genome profiling and matched anticancer treatment could be a solution of overcoming time issue of anticancer drug development. This canonical approach will give a big challenge of understanding and interpreting big data to cancer biologists and clinicians.

ED01-3

GENOMIC PORTRAITS OF BREAST CANCER

Matthew J. Ellis

Division of Oncology, Section of Breast Oncology,
School of Medicine, Washington Univ., Siteman Cancer Center, U.S.A.

Pioneering work over ten years ago demonstrated that breast cancer is a spectrum of diseases at a molecular level and can be classified into four main subgroups on the basis of mRNA expression profiling: Luminal A, Luminal B, HER2-enriched and basal-like. More recently, a 50 gene model called the PAM50 has been developed to segregate individual tumors into these subtypes using single sample predictor methodology (J Clin Oncol 2009; 27: 1160-1167). The PAM50 was used as one of the organizing principles for the Cancer Genome Atlas (TCGA) to report extensive data on breast tumors by DNA copy number, gene expression analysis, DNA methylation patterns, microRNA sequencing and reverse phase proteins arrays. Consistent with the conclusion that the intrinsic subtypes should be viewed as different diseases large differences in the 'omics data sets were observed within each intrinsic subtype (Nature 2012; 486: 353-360 and Nature 2012; 490: 61-70). Furthermore, the frequencies of individual actionable aberrations were strongly influenced by intrinsic subtype. Functional analysis of these data are beginning to suggest new therapeutic approaches for the treatment of breast cancer (Cancer Discovery 2013: 3; 27-34), the most notable "low hanging fruit" of which are HER2 mutations in HER2 non-over-expressed tumors which are now the target of an ongoing neuratinib trial (Cancer Discovery 2013: 3; 224 227). Other areas of focus for discovery sequencing in advanced clinical trials include the CDK4/CyclinD pathway and the PI3K pathway. However there are currently no clinically validated predictive biomarkers for the use of CDK4 inhibitors, rapalogs or other PI3 kinase inhibitors so that these agents are still being developed in populations defined only by ER and HER2 status. The problem here is that unlike one gene one drug paradigm pathway exemplified by our HER2 mutation/ neuratinib study, CDK 4/6 inhibitors and PI3 kinase inhibitors target complex multigene mutational spectra and we have yet to secure algorithms that can put multiple genes in a pathway into a common predictor (PLoS One 2013; 8: e67980). Ultimately the cure of epithelial malignancies will require a more sophisticated approach, whereby all the relevant biological parameters in a tumor are assessed as prelude to treatment. Increasingly sophisticated cancer informatics programs have been developed that place genomic data into the context of well-curated signaling and functional pathways to create networks, "interactomes" and "activitomes" (Clin Cancer Res 2013; 19: 3114-3120). While specific biological processes can then be linked to clinical phenotypes, these programs require multiple examples of each class for statistical inference, i.e. they have not reached the point of diagnosing a druggable pathway activation event in an individual patient.

Individualized and integrated analysis of DNA, RNA and Protein/Post translational modifications is therefore the next technical challenge in cancer diagnostics.

ED02-1

TCGA, THE BIG DATA FOR BREAST CANCER? INTRODUCTION AND METHOD FOR DATA MINING

Ju Han Kim

Division of Bimedical Informatics, College of Medicine, Seoul National Univ., Korea

Cancer is a complex disease, which can be dysregulated through multiple mechanisms. Thus, no single level of genomic data fully elucidates tumor behavior since there are many genomic variations within/between levels in a biological system such as copy number alterations, DNA methylation, alternative splicing, miRNA regulation, post translational modification, etc. Nowadays, a number of heterogeneous types of data have become more available from the Cancer Genome Atlas (TCGA), generating multiple molecular levels of omics dimensions from genome to phenome. Given multi-omics data, information from one level to another may lead to some clues that help to uncover an unknown biological knowledge. Thus, integration of different levels of data can aid in extracting new knowledge by drawing an integrative conclusion from many pieces of information collected from diverse types of genomic data. Previously, we have proposed a graph-based framework that integrates multi-omics data including copy number alteration, DNA methylation, gene expression, and miRNA expression, for cancer clinical outcome prediction. Genomic features do not act in isolation, but rather interact with other genomic features in complex signaling or regulatory networks since cancer is caused by the deregulation of alteration in pathways or complete processes. Thus, it would be desirable to incorporate genomic knowledge when integrating multi-omics data for cancer clinical outcome prediction. Here, we proposed a new method for integrating different levels of genomic data and genomic knowledge at hand in order to improve the predictive power and provide an enhanced global view on the interplay between levels. With integration of multi-omics data and genomic knowledge, understanding the molecular pathogenesis and underlying biology in cancer is expected to provide better guidance for improved diagnostic and prognostic indicators and effective therapies.

ED02-2

GENOMIC APPROACHES TO OVERCOME LIMITATION IN TISSUE ACCESS AND TUMOR HETEROGENEITY

Woong-Yang Park

Dept. of Molecular Cell Biology, School of Medicine, Samsung Medical Center; Sungkyunkwan Univ., Korea

Recent advances in genomics technologies over the last few years allowed us to understand the molecular and functional characteristics on human disease. Especially next generation sequencing (NGS) technologies made the big impact on genetic diseases such as Mendelian diseases and cancer. Targeted exome sequencing on actionable targets against cancer will be the first line genetic diagnosis of cancer patients. Many reports on the genome-wide analysis on the common diseases will help us to find the predictive biomarkers of the genetic susceptibility of cancers. Cellular heterogeneity within a tumor tissue is a widespread event. Stochastic gene and protein expression at the single cell level has been clearly demonstrated in different systems using a variety of techniques. Therefore, single cell analysis will lead to a more accurate representation of cell-to-cell variations instead of the stochastic average masked by bulk measurements. To understand fully the cellular specificity and complexity of tissue microenvironments under physiological conditions, it is necessary to measure molecular signatures with single cell resolution. Another category of new biomarker is circulating tumor DNA with patient-specific sequence signatures. Circulating tumor DNA is found in exosomal fraction of blood, representing a variable and generally small fraction of the total circulating DNA. Together with the advanced sequencing technologies we can rapidly identify somatic genomic alterations in individual tumors, and these can be used to design personalized assays for the monitoring of circulating tumor DNA. NGS technologies initiated the revolution in the medical field, and translational genomics research will be followed to accomplish the personalized medicine in a near future.

ED02-3

CLINICAL TRIALS BASED ON GENOMICS DATA MINING

Iain Tan Bee Huat

Dept. of Medical Oncology, National Cancer Centre Singapore, Singapore

Next Generation Genomics technologies have advanced at unprecedented speed. New Emerging technologies are available that can characterize patient samples at very high throughput providing high dimensional data that can be mined to discover predictive biomarkers or biomarkers of mechanisms of drug resistance. I will review some of these technologies as well as innovative trial designs that exploit these technologies for therapeutic evaluation.

ED03-1

ADVANCES IN SUPPORTIVE CARE : CLINICAL UPDATE

Soohyeon Lee

Division of Medical Oncology, Dept. of Internal Medicine, Yonsei Univ. Severance hospital, Korea

As researchers gain a better understanding of the toxicities associated with chemotherapy and radiation therapy, they have focused more on developing drugs and therapeutics that address the complications of cancer treatment.
One of the most important advancements in cancer treatment has been recognizing that supportive care and symptom management are key, regardless of the stage of disease or intent of treatment. More specifically, there is greater data demonstrating that the provision of supportive care, for example palliative care, can improve the experience of cancer patients. Another major advance is in the integration of palliative care and hospice into usual care. This is now recommended by the American Society of Clinical Oncology for anyone with serious cancer. Research indicates that care with both an oncology and a palliative care team can lead to better symptom management, improved communication, less depression and better understanding of the illness and options.

Clinical Update Refractory pain For the management of chronic uncontrolled pain related to cancer or its treatment, ketamine is widely used off label at subanesthetic doses for cancer pain, usually in conjunction with opioids. In the multicenter, dose-escalation, double-blind, randomized, placebo-controlled phase III trial, ketamine or placebo was delivered subcutaneously over 3 to 5 days. 185 participants were included in this study. There was no significant defference between the proportion of positive outcomes in the placebo and intervention arms (response rates, 27% and 31%). Those was almost twice the incidence of adverse events worse than baseline in the ketamine group after day 1 and throughout the study. Ketamine does not have net clinical benefit when used as an adjunct to opioids and standard coanalgesics in cancer pain while significantly increasing toxicity.

Sleep quality among cancer survivors 30-90% of cancer survivors report impaired sleep quality post-treatment, which can be severe enough to increase morbidity and mortality. Lifestyle interventions, such as exercise, are recommended in conjunction with drugs and cognitive behavioral therapy for the treatment of impaired sleep. 410 survivors were accrued. Participants attended tow 75-minute sessions per week. Sleep quality was assessed by using the Pittsburgh Sleep Quality Index and actigraphy pre- and postintervention. The yoga intervention used the Yoga for Cancer Survivors (YOCAS) program is a useful treatment for improving sleep quality and reducing sleep medication use among cancer survivors.
Malignant bowel Obstruction Bowel obstruction is often the terminal complication of advanced abdominal cancer, and can persist for several weeks or months until the patient dies. The obstruction gives rise to a vicous cycle of increased intestinal secretions and fluid accumulation, distension, and peristaltic activity, with the resultant damage to the intestinal epithelium eliciting an inflammatory response. To investigate the somatostatin analog lanreoride as symptomatic treatment for inoperable bowel obstruction due to peritoneal carecinomatosis, 80 patients with peritoneal carcinomatosis, two or more vomiting episodes per day or nasogastric tube who were previously treated with intravenous

corticosteroids and proton pump inhibitors were recruited. They were randomly assigned to one 30mg injection of lanreotide microparticles or placebo in a 10-day, bouble-blind, parallel-group phase. Primary endpoint was the proportion of patients responding on day 7 (one or fewer episodes of vomiting per day or no vomiting recurrence after NGT removal). More patients receiving lanreoride than placebo were responders. Improvements in well-being were significantly greater with lanreotide on days 3, 6, and 7. Lanreotide has some efficacy and is safe in the symptomatic treatment of patients with inoperable bowel obstruction due to peritoneal carcinomatosis. Denosumab for Bone metastasis Denosumab was found to be more effective in delaying the time to first SRE and reducing the risk of first and subsequent SRE compared to zoledronic acid, placebo and pamidronate. In breast and prostate cancer, denosumab was effective in reducing skeletal morbidity rate compared with placebo. The lack of published data on pain and QoL meant that firm conclusions could not be made. Denosumab did not appear to have an affect on overall survival.

Guidelines on antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy Antibacterial and antifungal prophylaxis are only recommended for patients expected to have <100 neutrophils/uL for> 7 days, unless other factors increase risks for complications or mortality to similar levels. According to validated risk index, patients with MASCC scorese≥21 0r in Talcott group 4, and without other risk factors, can be managed safely as outpatients. Febrile neutropenic patients should receive initial dose of empirical antibacterial therapy within an hour of triage and should either be monitored for at least 4 hours to determine suitability for outpatient management or be admitted to the hospital. An oral fluoroquinolone plus amoxicillin/clavulante (or plus clindamycin if penicillin allergic) is recommended as empiric therapy, unless fluoroquinolone porphylaxis was used before fever developed.

ED03-2

ADVANCES IN ONCOLOGY NURSING - HEREDITARY BREAST CANCER: EDUCATION & RESEARCH

Kyung Hee Lim

Dept. of Nursing, College of Nursing, Keimyung Univ., Korea

Breast cancer ranks as the second prevalent form of cancer among Korean female population. It is estimated that approximately 5-10% of all breast cancer cases are associated with genetic predisposition. Recently, interest in hereditary breast cancer has increased rapidly among all health care providers as well as the laity. Given this situation, there have been ongoing developments in cancer genetic risk assessment and management at primary, secondary, and tertiary levels of care since the breast cancer susceptibility genes BRCA 1 and BRCA 2 were identified in 1994. In order to provide individualized care at various levels to patients with hereditary breast cancer or persons at high risk for hereditary breast cancer, it is important to provide oncology nurses relevant education focusing on in-depth knowledge, advanced nursing and genetic counseling skills related to hereditary breast cancer. Some oncology nurses interested in hereditary breast cancer have been trained through special education programs highlighting significant concepts and palliative measures on hereditary breast cancer such as risk-reduction strategies and management (i.e. prognostic factors and pathology, surgery, radiation therapy, systemic therapy), environmental modifiers, genetic counseling and ethical issues in genetics related to hereditary breast cancer. Besides those trained roles, oncology nurses are now required to play additional role in identifying factors affecting psychosocial problems among patients with hereditary breast cancer and to employ therapeutic communication skills not only to comprehensively assess patients but also to adequately provide information regarding hereditary breast cancer. In addition, family members' need for specific information and support about their individual risk status and any subsequent risk management should be taken into consideration as there has been increase in media reporting family members' risk for hereditary breast cancer, thus provision of adequate education program for family members should be also highly regarded.

The recent explosion of hereditary breast cancer genetic research has broadened our perspective and understanding of genetic influences on health and disease. These researches have investigated psychological distress, anxiety, depression, risk perception, knowledge, and concern of patients and clients at high risk for hereditary breast cancer. Furthermore, some recent studies have documented relevant input regarding impacts of genetic counseling, communication of genetic risk and risk assessment. In addition, multiple studies have explored risk factors and surveillance behaviors for hereditary breast cancer and decision-making process for prophylactic surgery. These scientific advances have significant implications for clinical oncology nurses and advanced practice nurses. Compared with trends in research worldwide, limited nursing research on hereditary breast cancer is found in Korea. Research-based evidence can provide oncology nurses with advanced nursing knowledge and skills to establish a holistic plan of care for clients with an actual or potential genetic risk for breast cancer, thus it is imperative to perform substantial and relevant research on hereditary breast cancer in Korea.

ED03-3

CONSTRUCTION AND INTERPRETATION PEDIGREE

Bo Kyoung Ku

Dept. of Nursing, ASAN medical center, Korea

The basis of the successful genetic counseling is to collect basic data including family history accurately. It is helpful diagnosis of a hereditary cancer syndrome and identify the suitability of the recommendation for a genetic testing, medical treatment, cancer risk reduction and a demand for a checkup through the family history.

1. pedigree

A pedigree is a diagram which the family history is schematized to be organized in a standardized form. The biological kinship between a proband is expressed as symbols, vertical and horizontal lines in a pedigree. The diseased state is shown as oblique strokes and abbreviations.

2. Proband

A client is the first individual who makes a request for genetic counseling.

3. Family History including three generations

The family history including three generation is to include the proband's first degree family (brothers, sisters, children and parents), second degree family (half brothers and sisters, nephews and nieces) and third degree family (cousins).

4. Treatment History

It is desirable to record all the contents of surgical treatments which members with and without cancer had in drawing a cancer pedigree. It is needed to include all treatments such as therapeutic surgeries (surgical history of breast, ovarian, prostate or other cancers), prophylactic surgeries (hysterectomy, ovariotomy or mastectomy) and surgeries for the treatment of benign diseases (resection of skin lesions and melanoma). When a medical examination is made for every member's cancer history, it is helpful to identify whether the affected cancer is cancer precursor lesions, primary or metastatic cancer.

5. Race and Ethnic Group

It is necessary to record racial and ethnic information. The susceptibility of hereditary breast cancer can be evaluated and a difference can be placed on mutation inspection techniques according to the types of ethnic groups.

6. Preparation for a Pedigree and Standardized Symbols

Symbols, definitions and abbreviations used in a pedigree are shown in <Figure 1 & 2>.

Instructions:
— Key should contain all information relevant to interpretation of pedigree (e.g., define fill/shading)
— For clinical (non-published) pedigrees include:
  a) name of proband/consultand
  b) family names/initials of relatives for identification, as appropriate
  c) name and title of person recording pedigree
  d) historian (person relaying family history information)
  e) date of intake/update
  f) reason for taking pedigree (e.g., abnormal ultrasound, familial cancer, developmental delay, etc.)
  g) ancestry of both sides of family
— Recommended order of information placed below symbol (or to lower right)
  a) age; can note year of birth (e.g., b.1978) and/or death (e.g., d. 2007)
  b) evaluation (see Figure 4)
  c) pedigree number (e.g., I-1, I-2, I-3)
— Limit identifying information to maintain confidentiality and privacy

	Male	Female	Gender not specified	Comments
1. Individual	b. 1925	30y	4 mo	Assign gender by phenotype (see text for disorders of sex development, etc.). Do not write age in symbol.
2. Affected individual				Key/legend used to define shading or other fill (e.g., hatches, dots, etc.). Use only when individual is clinically affected.
				With ≥2 conditions, the individual's symbol can be partitioned accordingly, each segment shaded with a different fill and defined in legend.
3. Multiple individuals, number known	5	5	5	Number of siblings written inside symbol. (Affected individuals should not be grouped).
4. Multiple individuals, number unknown or unstated	n	n	n	"n" used in place of "?".
5. Deceased individual	d. 35	d. 4 mo	d. 60's	Indicate cause of death if known. Do not use a cross (†)to indicate death to avoid confusion with evaluation positive (+).
6. Consultand				Individual(s) seeking genetic counseling/ testing.
7. Proband	P	P		An affected family member coming to medical attention independent of other family members.
8.Stillbirth (SB)	SB 28 wk	SB 30 wk	SB 34 wk	Include gestational age and karyotype, if known.
9. Pregnancy (P)	P LMP: 7/1/2007 47,XY,+21	P 20 wk 46,XX	P	Gestational age and karyotype below symbol. Light shading can be used for affected; define in key/legend.

Figure 1

1. Definitions	Comments
1. relationship line, 2. line of descent, 3. sibship line, 4. individual's line	If possible, male partner should be to left of female partner on relationship line. Siblings should be listed from left to right in birth order (oldest to youngest).
2. Relationship line (horizontal)	
a. Relationships	A break in a relationship line indicates the relationship no longer exists. Multiple previous partners do not need to be shown if they do not affect genetic assessment.
b. Consanguinity	If degree of relationship not obvious from pedigree, it should be stated (e.g., third cousins) above relationship line.
3. Line of descent (vertical or diagonal)	
a. Genetic	Biologic parents shown.
- Multiple gestation	Monozygotic; Dizygotic; Unknown; Trizygotic. The horizontal line indicating monozygosity is placed between the individual's line and not between each symbol. An asterisk (*) can be used if zygosity proven.
- Family history not available/ known for individual	? ?
- No children by choice or reason unknown	or (vasectomy, tubal). Indicate reason, if known.
- Infertility	or (azoospermia, endometriosis). Indicate reason, if known.
b. Adoption	in; out; by relative. Brackets used for all adoptions. Adoptive and biological parents denoted by dashed and solid lines of descent, respectively.

Figure 2

ED04-1

ADVANCES IN MEDICAL ONCOLOGY

Young-Hyuck Im

Dept. of Hematology-Oncology, Samsung Medical Center, Korea

Breast cancer is a group of heterogeneous diseases which have substantial variation in their clinical and molecular characteristics. Molecular profiling of breast cancer by gene expression studies has provided us an important tool to discriminate and categorize a number of subtypes. These breast cancer subtypes by gene expression profiling have been shown to be associated with clinical outcome and treatment response. Recently, rapid progress in the field of cancer genomics through massive parallel or high throughput next generation sequencing has been made in understanding the genomic diversity of breast cancer. These advances led to the characterization of a new genome-driven integrated classification of breast cancer, which refines the existing classification systems currently used. Cancer genomics has already revolutionized our knowledge of breast cancer molecular pathology, enabling us to develop new and more effective treatment. Specific biological processes and distinct gene pathways are associated with prognosis and sensitivity to chemotherapy and targeted agents in different subtypes of breast cancers. The identification of functional pathways that are enriched for mutated genes can select sub-population of patients who will most likely be sensitive to biology driven targeted agents. The selection of driver pathways in resistant tumors will permit to discover a biology-driven platform for new drug development to overcome resistance. These findings have profound implications both for the individualization of treatment approaches, bringing us a step closer to the realization of personalized cancer care in breast cancer, but also provide a new framework for studying the underlying biology of each novel subtype.

This review will focus on the most recent advances in the new emerging agents targeting the driver pathways within breast cancer molecular subtypes, and recent progress in trials of systemic therapies, including endocrine therapy, chemotherapy and targeted therapies for breast cancer.

ED04-2

ADVANCES IN TRANSLATIONAL RESEARCH

Yoon-La Choi

Dept. of Pathology, Samsung Medical Center, Korea

The field of translational research and the transition of laboratory findings from the bench to the clinic in the field of breast oncology include new sequencing data of breast cancers, as well as the multigene signatures and patient-derived xenograft model for personalized medicine.

All cancers carry somatic mutations. The patterns of mutation in cancer genomes reflect the DNA damage and repair processes to which cancer cells and their precursors have been exposed. Recently, the genomes of breast cancers sequencing showed remarkable phenomenon of localized hypermutation, termed kataegis. Regions of kataegis differed between cancers but usually colocalized with somatic rearrangements. The next-generation sequencing (NGS) is revolutionizing the field of personalized cancer diagnostics and medicine. In this study, we performed genetic mutation analysis of Korean triple negative breast cancer samples using HaloPlex enrichment system-based targeted next-generation sequencing. Exons of 368 breast cancer-associated genes were captured and sequenced in mean target coverage depth of 150X. Among the targeted 368 genes, 198 harbor 630 somatic non-synonymous SNVs and 45 INDELs. Most frequently mutated genes were TP5, MLL3, POU5F1B, and ARAF. Taken together, our study reveals the causative oncogenes underlying Korean triple negative breast cancer and establishes new NGS-based targeted platform for identifying mutations causing cancer.

Although breast cancer cell lines are widely used for mechanistic and therapeutic studies due to their well-defined characteristics, they do not adequately reflect breast cancer heterogeneity or morphology, thus limiting their predictive value. Furthermore, most breast cancer cell lines when orthotopically injected do not efficiently metastasize and require tail vein injection to generate contrived metastatic models. In contrast, patient-derived xenograft (PDX)s retain the morphology, cellular heterogeneity, and molecular profiles of the original patient tumors, thereby being relevant preclinical models to identify effective therapeutic regimens that can be translated into clinical practice. PDXs recapitulate the heterogeneity of treatment response as seen in the clinic and show concordance with the original patient's treatment response. Personalized medicine is intended to select subsets of patients that will most likely respond to treatment regimens, thus reducing morbidity and mortality from ineffective treatments. To identify targeted therapies and effective treatment regimens based on subtype classification, representative breast tumor PDXs can be assigned to each arm of a preclinical clinical trial. In the near future, the knowledge gained by the ongoing efforts of genomic classification from complete genome sequencing of patient tumors and PDX is expected to drive the next generation of preclinical clinical trials aimed to personalizing cancer therapy.

ED05-1

ADVANCES IN BREAST SURGERY

Ho Yong Park

Dept. of Breast Surgery, Kyungpook National Univ. Medical Center, Korea

Oncoplastic surgery has revolutionized the field of breast conserving surgery (BCS). The final aims of this technique are to obtain an adequate resection margin that will reduce the rate of local recurrence while simultaneously improving cosmetic outcomes. To obtain successful results after oncoplastic surgery, it is imperative that patients be risk-stratified based on risk factors associated with positive margins, that relevant imaging studies be reviewed, and that the confirmation of negative margins be confirmed during the initial operation. Patients who had small- to moderate-sized breasts are the most likely to be dissatisfied with the cosmetic outcome of surgery, even if the defect is small; therefore, oncoplastic surgery in this population is warranted. Reconstruction of the remaining breast tissue is divided into volume displacement and volume replacement techniques. The use of the various oncoplastic surgeries is based on tumor location and excised breast volume. If the excised volume is less than 100 g, the tumor location is used to determine which technique should be used, with the most commonly used technique being volume displacement. However, if the excised volume is greater than 100 g, the volume replacement method is generally used, and in cases where more than 150 g is excised, the latissimus dorsi myocutaneous flap may be used to obtain a pleasing cosmetic result. The local recurrence rate after oncoplastic surgery was lower than that of conventional BCS, as oncoplastic surgery reduced the rate of positive resection margins by resecting a wider section of glandular tissue. If the surgeon understands the advantages and disadvantages of oncoplastic surgery, and the multidisciplinary breast team is able to successfully collaborate, then the success rate of BCS with partial breast reconstruction can be increased while also yielding a cosmetically appealing outcome. There are some limitations for breast conserving surgery. For these cases, Skin sparing or Nipple-sparing mastectomy (NSM) improves cosmetic results after mastectomy. As most consider advanced tumors, or tumors near the nipple-areola complex (NAC), as a contraindication for this type of surgery, many doctors tried to solve these problems. Nipple-sparing mastectomy (NSM) is increasingly offered to women for therapeutic and prophylactic indications. The reconstruction was performed with autologous tissue, tissue expander and implant-expander. Success depends on coordinated planning with the oncologic surgeon and careful preoperative and intraoperative management. Conservative surgery represents the target of current breast cancer treatment where possible, and skin-sparing mastectomy an interesting alternative to classical one when radicality is required.

Table 1. Partial mastectomy reconstruction techniques

Volume displacement techniques	Volume replacement techniques
Glandular reshaping	Local flaps
Linear suture	Adiposfascial flap
Parallelogram mastopexy Lumpectomy	Lateral thoracodorsal flap
Purse-string suture	Thoracoepigastric flap
Round block technique	ICAP flap
Batwing mastopexy	Distant flaps
Tennis racket method	TDAP flap
Rotation flap	LD myocutaneous flaps
Reduction mammoplasty techniques	
Inverted T	
Vertical type	

ICAP = intercostal artery perforator; TDAP = thoracodorsal artery perforator; LD = latissimus dorsi.

Table 1

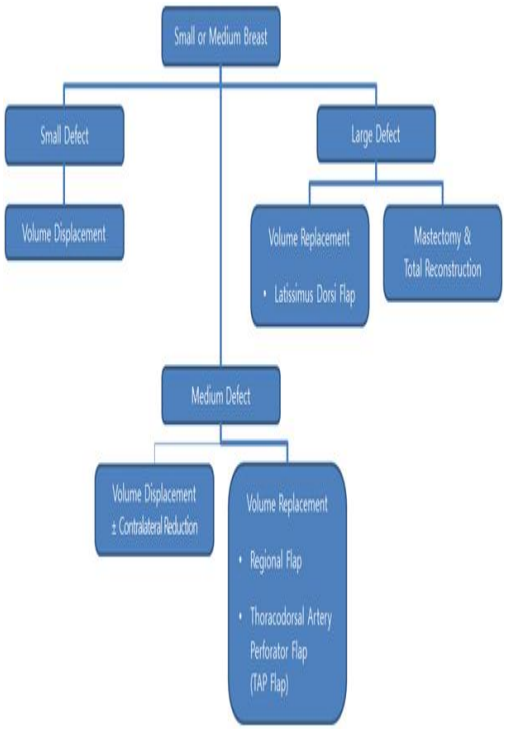

Figure 1

ED05-2

HER2 HETEROGENEITY IN BREAST CANCER

So Yeon Park

Dept. of Pathology, College of Medicine, Seoul National Univ. Bundang Hospital, Korea

HER2 status had been considered relatively homogeneous across all cells within a tumor and constant during the progression of breast cancer, suggesting that anti-HER2 therapy would successfully target most of the tumor cells in patients with HER2-positive breast cancer. However, there is increasing recognition of intra-tumoral heterogeneity of HER2 expression and HER2 amplification in a significant proportion of breast cancers. In a previous study, intra-tumoral heterogeneity of HER2 amplification was identified in a subset of HER2-positive breast cancers and HER2 heterogeneity was found to an independent predictor of poor prognosis in patients with primary HER2-postive breast cancer. However, the importance of intra-tumoral HER2 heterogeneity lies in not only its hindrance to accurate assessment of HER2 status or its prognostic significance but also its possible association with treatment response to HER2-targeted therapy. In a further study, HER2 regional heterogeneity was found to be a negative predictor of trastuzumab response in patients with HER2-positive metastatic breast cancer. Moreover, tumors with low level amplification and tumors where a small proportion of cells had a HER2/CEP17 ratio >2.2 or a HER2 IHC score of 3+ were clearly less responsive to trastuzumab-based chemotherapy. An obvious clinical implication of these findings is that patients with heterogeneously amplified HER2-positive breast cancer are less likely to benefit from trastuzumab therapy. Thus, HER2 in situ hybridization results should include detailed information about HER2 heterogeneity, e.g. the proportion of tumor cells with a HER2/CEP17 ratio >2.2, degree of overall HER2/CEP17 ratio, and regional heterogeneity.

ED06-1

ADVANCES IN RADIOLOGY

Sung Hun Kim

Dept. of Radiology, Seoul St. Mary's Hospital, Korea

Tomosynthesis

Digital breast tomosynthesis enables the acquisition of 3D volume of thin section data and images are reconstructed in conventional orientations by using reconstruction algorithms similar to those used in CT. Tomosynthesis has been shown to increase the conspicuity of many lesions while reducing false-positive findings from summation of overlapping tissue, resulting in better sensitivity in small cancer detection. It can lower the recall rates.

Elastography

Breast ultrasound elasticity evaluation has become a routine tool in addition to diagnostic ultrasound during the last five years. Revised ACR BI-RADS®-US will include tissue stiffness assessment (soft, intermediate and hard) by elastography. Quantification was disallowed by FDA, but is ready to be updated when numerical scale is approved.

Three different modes are currently available in tissue elastography: Free-hand ultrasound elastography, The Acoustic Radiation Force Impulse (ARFI) technique, Shear-wave elastography.

1) Clinical Application

A) Usefulness of breast elastography for characterizing solid lesions

Most of the recent published studies show that these different elasticity modes help differentiate benign and malignant solid breast lesions. Solid malignant lesions are usually stiffer than solid benign lesions. The functional information provided by elasticity evaluation is more useful for atypical benign or malignant lesions (BI-RADS 3 or 4a). Some studies show that the biopsy rate could be reduced in case of BI-RADS 3-4a benign lesions in women with a high risk of breast cancer. Elasticity combined with B-mode imaging could improve specificity up to 75-77%. Nevertheless, false negatives do arise. Typical false negative lesions are “soft” lesions such as mucinous carcinoma, cystic carcinoma or inflammatory cancer. Thus, B-mode features are usually suspicious enough to categorize these lesions as BI-RADS 4b or 5. False positives can occur in fibrous benign lesion such as “old” fibroadenoma.

Automated Breast Ultrasonography

The automated whole ultrasonography (AWUS) scanners were originally designed to effectively examine the entire breast and to overcome the operator dependency of the hand held US (HHUS).The current high-resolution AWUS scanners with volumetric technologies can demonstrate the breast anatomy and document the breast lesions.Several studies have shown the good diagnostic performance and good interobserver agreement between the volumetric AWUS and the HHUS.

AWUS has several advantages over HHUS; (1) it is more reproducible, and it allows a thorough imaging of the entire breast, (2) it has higher definition, better contrast and sharpness and smaller images for review due to a high-resolution 2000-line reading monitor with a 3D capability, (3) it allows displayed interpretation at computer-monitor-based reading stations with non-real-time review, which optimises the radiologist’s reading environment and (4) it is well accepted by participants because of

the reduced breast compression (compared to that of the MMG), the lack of exposure to ionizing radiation and the lack of contrast medium injection. Therefore, the high-resolution AWUS scanners are good for follow-up studies, and they can improve the confidence level of a negative reading.
Detection rate of intraductal tumor or fine details of microcalcifications was better in HHUS than in AWUS, that of cystic lesion or focal fibrosis was better in AWUS than in HHUS. There was silimilar detection rate of solid masses.

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ED06-2

ADVANCES IN RADIATION ONCOLOGY

Yong Bae Kim

Dept. of Radiation Oncology, Yonsei Univ. Severance Hospital, Korea

Radiotherapy for breast cancer patients has entered upon the new phase since the paradigm shift of computed tomography (CT) based treatment planning in the 2000's from conventional two dimensional radiation treatment planning in the 1990's. In Korea, most RT units have equipped CT based treatment planning systems since the late 2000's. Therefore, it is getting clinically more important to define normal organs such as, breast, chest wall, regional node, lung, and heart and make a practical treatment planning system. There are two definitions released by Radiation Therapy Oncology Group and Danish Breast Cancer Cooperative Group until now [1,2].

After defining normal and target organs on CT slices, the next step is to make a treatment plan. The goal of radiation treatment planning is generally thought to deliver homogenous radiation dose to target organ and minimize irradiation to normal organs. Irradiated dose to breast/chest wall and regional node is recommended from 95 to 107% and 90 to 107% of prescribed dose. As well, there is no guideline to define tumor bed for boost irradiation that has been paid attention because of accelerated partial breast irradiation (APBI) as an alternative to conventional whole breast irradiation for early indolent breast cancer patients. The study have been investigated so far to improve target delineation in APBI delivered by conformal external beam radiation therapy, including the use of standardized guidelines, surgical clips or fiducial markers, pre-operative computed tomography imaging, and additional imaging modalities, including magnetic resonance imaging, ultrasound imaging, and positron emission tomography/computed tomography [3].

Recently, several studies were published to investigate radiotherapy-induced cardiotoxicity in breast cancer patients [4,5]. Nilsson et al. reported an increase of stenosis in mid and distal left anterior descending artery and distal diagonal in irradiated left-sided breast cancer and an association between high-risk RT and stenosis in hotspot areas for radiation indicate a direct link between radiation and location of coronary stenosis. Darby et al. performed a population-based case-control study of major coronary events in Sweden and Denmark patients. The study demonstrated that exposure of the heart to ionizing radiation during radiotherapy for breast cancer increases the subsequent rate of ischemic heart disease proportionally to the mean dose to the heart, begins within a few years after exposure, and continues for at least 20 years. Therefore, it becomes the important clinical issue to reduce the risks of cardiac disease associated with radiotherapy in patients with breast cancer. Several methodologies can be clinically applied to lower the irradiated dose to heart [6]. CT-based planning is essential to design fields and beam arrangement to minimize cardiac exposure. Immobilization devices and novel image-guided techniques can reduce interfractional and intrafractional variations. Additionally, breath-hold technique can be used to displace the heart out of the radiation field. Prone position can be also used to displace breast away from the anterior chest wall. IMRT and proton therapy may be suggested as a means to reduce cardiac exposure dose.

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Free Paper

FP01-1

ATTITUDE TOWARDS PERFORMING BREAST SELF-EXAMINATION (BSE) AMONG FEMALE UNDERGRADUATES IN HONG KONG

Chung Yin Joyce Leung*, Hin Ting Tsang, Ting Ting Wong, Wing Sze Shum, Ka Man Leung, Hiu Ching Mak, Wai Hang Mok, Sin Yu Tai, Yat Kwan Alan Tsang

Division of Nursing & Health Studies, The Open Univ. of Hong Kong, Hong Kong

Background/Purpose：Breast cancer is the most common cancer among women in Hong Kong, in which it was the third leading cause of cancer deaths among female in 2009. In one in every 19 women, they have a chance of developing breast cancer by the age of 75. Breast cancer is not an age-related disease and young age women are without exception. The median age of breast cancer patients in Hong Kong are the youngest compared to other countries. Breast self-examination (BSE) is an economic, simple and non-invasive method of breast cancer screening. Early detection and treatment of breast cancer not only increase the survival rate, but also enhance a better prognosis as well as better medical resources allocation. In this study, relationship between religion, family history of breast related problems, personal history of breast related problems, resources of BSE information and BSE education, and the attitude of BSE, were investigated among female undergraduates in Hong Kong.

Methods：A cross-sectional descriptive study design was adopted. Convenience sampling was used to invite female undergraduates in Hong Kong to participate in this study. A self-administered questionnaire consisted of two parts: demographic data about religion, family history, personal history, resources of information and educations, and the questionnaire “Attitude about Breast Self-Examination”. Descriptive and parametric tests were used to illustrate the relationship between religion, family history and personal history of breast related problems, resources of BSE information and BSE education and the attitude of BSE among the female undergraduates in Hong Kong.

Results：A total of 274 questionnaires returned (response rate=91.13%). There was no significant difference in the mean scores of the “Attitude about Breast Self-Examination” among the participants with religion or without religion, with or without family history of breast related problems and participants with or without personal history of breast related problems. Significant difference found between participants who had BSE information obtained and those had no BSE information obtained. The mean score of participants who had BSE information obtained was 72.00+7.30 and those had no BSE information obtained was 67.53+6.90 ($t(272)=5.18$, $p<0.01$, two-tailed). Furthermore, there was significant difference found among participants who received BSE education and those did not received BSE education, with mean score 71.55 + 7.56 and 68.69 + 7.21 respectively ($t(272)=2.86$, $p<0.01$, two-tailed).

Conclusion：The study showed that female undergraduates in Hong Kong showed positive attitude towards performing BSE unless they had obtained BSE information or received BSE related education previously. This suggested health promotion of BSE as a screening method of breast cancer should be implemented in health education sessions either in school curriculum or community, so as promoted through mass media at young age of women.

FP01-2

MAMMOGRAPHIC DENSITY AS A BREAST CANCER RISK PREDICTOR ASSOCIATED WITH ESTRADIOL LEVEL AND BODY MASS INDEX IN INDONESIAN WOMEN

Lina Choridah[1*], **Teguh Aryandono**[2], **Arif Faisal**[1], **Ahmad Hamim Sadewa**[3]

[1] *Dept. of Radiology, Faculty of Medicine Universitas Gadjah Mada, Indonesia*
[2] *Dept. of Oncology Surgery, Faculty of Medicine Universitas Gadjah Mada, Indonesia*
[3] *Dept. of Biochemistry, Faculty of Medicine Universitas Gadjah Mada, Indonesia*

Background/Purpose : Breast cancer is the leading cause of women cancer morbidity and mortality worldwide and in Indonesia. The incidence rate continuously each year therefore breast cancer becomes one of the major health problems in Indonesia. Mammographic density reflects the number of stromal and epithelial. Women with denser mammographic density have a higher risk of breast cancer. Mammographic density is influenced by some hormones and growth factors. Estrogen is believed to play an important role in both mammographic density and BMI, but the detailed mechanism of the induction process of mammary carcinogenesis is not fully understood. The main estrogen produced in women is estradiol. The purpose of this research is to examine association between mammographic density as breast cancer predictor, estradiol level, and BMI.

Methods : This was an observational study, data were collected prospectively using cohort study design. Subjects were women who came to undergo screening mammography in Kotabaru Oncology Clinic, Yogyakarta, Indonesia. Analog mammogram was digitilized, mammographic density was asses using thresholding method. Estradiol was asses using ECLIA (Electrochemiluminescence Immunoassay). The data were analyzed using logistic regression and correlation.

Results : There were 120 subjects, 60 subjects is a breast cancer survivor and 60 without breast cancer. Women with 25%-34 %, 35%-49%; 50%-64%; and > 65% percentage mammographic density have a relative risk 1,667 (95% CI 0.47-5.89), 3,4 (95% CI 1.16-9.97), 3,43 (95% CI 1.19-9.88) and 3,45 (95%CI 1.174-10.14) compare with <25% percentage mammogramphic density. Estradiol have a positive correlation with mammographic density in both premenopausal (r=0.285, p=0.014) and postmenopausal women (r=0.181, p=0.228). Among premenopausal women correlation analyzes showed a strong inverse association of BMI on estradiol level and mammographic density. By contrast, in postmenopausal, BMI presents a positive correlation on estradiol level and no significant negative correlation with mammographic density. BMI >25 kg/m^2 had an odds ratio by 2.382 (95% CI 0.970-5.849), on multivariate analysis without adjustment of mammographic density, and an odds ratio increased by 3.542 (95% CI 1.269-9.989) after adjustment.

Conclusion : Estrogenic effect is one of mechanism of mammographic density as breast cancer risk predictor. This research showed different interaction between percentage mammographic density, body mass index and estradiol level based on menopausal status. Estradiol in premenopausal women is produce by ovary and has negative correlation with BMI but in contrast, in postmenopausal, BMI contribute to produce estradiol by adipose tissue aromatization. The correlation between mammographic density, circulatory estrogen-level and body mass index in breast cancer risk should advance our understanding of breast cancer etiology and promotes primary prevention.

FP01-3

MAGNETIC RESONANCE IMAGING FINDING OF TRIPLE NEGATIVE BREAST CANCER

Sun Hyoung Shin, Young Jae Ryu, Min Jung Hwang,
Jin Seong Cho, Min Ho Park*, Jung Han Yoon

Dept. of Surgery, Chonnam National Univ. Hwasun Hospital, Korea

Background/Purpose : The objective of our study was to retrospectively evaluate the magnetic resonance(MR) imaging finding of "Triple-negative" breast cancer (ie, cancer that is estrogen receptor[ER] negative, progesterone receptor[PR] negative, and human epidermal growth factor receptor 2[HER2] negative) and to compare them with those of breast cancer that are luminal type and HER2 overexpression type.

Methods : From January 2010 to December 2012, MR imaging, mammography and ultrasound finding of 1055 patients with pathologically confirmed ER, PR and HER2 negative (triple negative, n=139), ER or PR positive/HER2 negative (luminal A, n=658), ER or PR positive/HER2 positive (luminal B, n=171), ER and PR negative/HER2 positive (HER2 overexpression type, n=87) were retrospectively reviewed. We also reviewed cancer stage, tumor type, histological grade, and the biological markers.

Results : Triple negative breast cancer was most commonly medullary cancer and high stage, showed a p53 positive (p=0.004) and Ki-67 positive (p<0.001), high histological grade (p<0.001). On MR imaging, triple negative breast cancers usually presented with a mass lesion type than segmental clumped non-mass like lesion (p=0.035). The mass lesion of triple negative breast cancer was presented with lobulated mass shape (0.001), rim enhancement (p<0.001) on MR imaging. On mammography and ultrasound, there was no distinction among the triple negative breast cancer and non-triple negative breast cancer.

Conclusion : Our results suggest that several MR imaging features might be useful for detecting triple negative breast cancer.

FP01-4

TIME INTERVAL FROM DIAGNOSIS TO TREATMENT IN INVASIVE BREAST CANCER PATIENTS

Haeseong Park[1], **Norma Kanarek**[2], **Antonio Wolff**[3], **Julie Lange**[4], **Kala Visvanathan**[5]

[1] *Division of Hematology Oncology and Palliative Care, Dept. of Internal Medicine, Virginia Commonwealth Univ., U.S.A.*

[2] *Dept. of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, U.S.A.*

[3] *Dept. of Oncology, Johns Hopkins Medical Institutions, U.S.A.*

[4] *Dept. of Surgery, Johns Hopkins Medical Institutions, U.S.A.*

[5] *Dept. of Breast Cancer, Johns Hopkins Medical Institutions, U.S.A.*

Background/Purpose : Postponement of mammography, ignorance of symptoms, and lengthened time to diagnosis are all segments of delay that may be experienced by the woman with breast cancer. Interval from diagnosis to treatment is reasonably an additional indicator of delay that may attribute to disparities in cancer outcome. We aimed to identify the factors that are associated with longer interval between diagnosis and treatment and further evaluate whether the lengthened interval is associated with poor survival outcomes in female breast cancer patients.

Methods : This is a retrospective cohort study using Johns Hopkins Hospital (JHH) Cancer Registry. We included patients with primary female invasive breast cancer diagnosed between 2000 and 2009 that received first course of treatment at JHH within 6 months of diagnosis. Patients with metastatic disease were excluded. Multiple linear regression was used to assess the association between patient characteristics and the interval from diagnosis to treatment. Cox proportional hazards models were used to calculate mortality hazard ratio, adjusted for patient characteristics (race, age at diagnosis, distance from hospital), tumor characteristics (stage, hormone receptor status), type of initial treatment, and use of adjuvant therapy.

Results : A total of 3,030 patients were reviewed. Caucasian patients had earlier stage disease and more hormone positive tumors compared to African-American patients, and had better survival outcomes. Mean interval from diagnosis to initial treatment in all patients was 44.4 days (95% confidence interval 43.4 - 45.4 days). African- American race was associated with lengthened interval of 51 days (95% CI 48.7 - 53.2) compared to Caucasian (42.5 days, 95% CI 41.4 - 43.7) with p-value <0.001 when adjusted for age at diagnosis, distance from hospital, stage at diagnosis and type of initial treatment. Lengthened interval beyond 2 months after diagnosis was not associated with worse survival outcome; however, African-American race still remained a poor prognostic factor for survival in this population (HR for mortality 1.43, 95% CI 1.12 - 1.83) when adjusted for the interval, age, distance from hospital, stage, hormone receptor status, and use of adjuvant therapy.

Conclusion：African-American patients experience longer delay to initial treatment after diagnosis of invasive breast cancer. However, lengthened diagnosis to treatment interval, defined as greater than two months between biopsy to first treatment, does not appear to have effect of survival outcomes in female breast cancer population. In this time of willingness to launch patient navigator programs to shorten intervals, changing the length of diagnosis to treatment interval alone may not result in improved outcomes in African American women, without fully understanding the sequence of matters taking place during this interval. This study of interval from diagnosis to initiation of treatment may serve as a pilot study to dissect and understand survival-relevant sequences of cancer care.

	Adjusted mean interval, Days (95% CI)	Difference compared to the reference group, Days (95%CI)	P-value
Total	44.4 (43.4 ~ 45.4)		NA
Race			
Caucasian	42.5 (41.4 ~ 43.7)	Reference	
African-American	51.0 (48.7 ~ 53.2)	8.0 (5.8 ~ 11.0)	<0.001
Age at diagnosis			0.003**
Less than 40	38.0 (34.8 ~ 41.2)	-6.4 (-10.1 ~ -2.8)	0.001
40 - 49	45.0 (43.1 ~ 46.9)	0.6 (-2.0 ~ 3.2)	0.65
50 - 59	44.4 (42.6 ~ 46.2)	Reference	
60 - 69	44.4 (42.3 ~ 46.5)	0 (-2.8 ~ 2.8)	1.0
70 and older	47.6 (44.9 ~ 50.2)	3.2 (0~6.3)	0.05
Distance from JHH			<0.001**
Baltimore City	43.2 (40.8 ~ 45.7)	Reference	
Baltimore Metro	39.8 (37.9 ~ 41.8)	-3.4 (-6.6 ~ -0.2)	0.04
Regional	45.6 (43.9 ~ 47.3)	2.4 (-0.6 ~ 5.4)	0.12
Other	48.6 (46.5 ~ 50.6)	5.3 (2.1 ~ 8.6)	0.001
Stage			0.03**
I	45.7 (44.2 ~ 47.1)	Reference	
II	43.9 (42.3 ~ 45.4)	-1.8 (-3.9 ~ 0.4)	0.11
III	41.5 (38.7 ~ 44.3)	-4.2 (-7.4 ~ -0.9)	0.01
Type of initial treatment			
Surgery	44.5 (43.4 ~ 45.6)	Reference	
Non-surgical treatment	43.8 (41.1 ~ 46.6)	-0.7 (-3.7 ~ 2.3)	0.66
*Each variable adjusted for all other variables in the table.			
**Wald test for group of categories			

Table 1

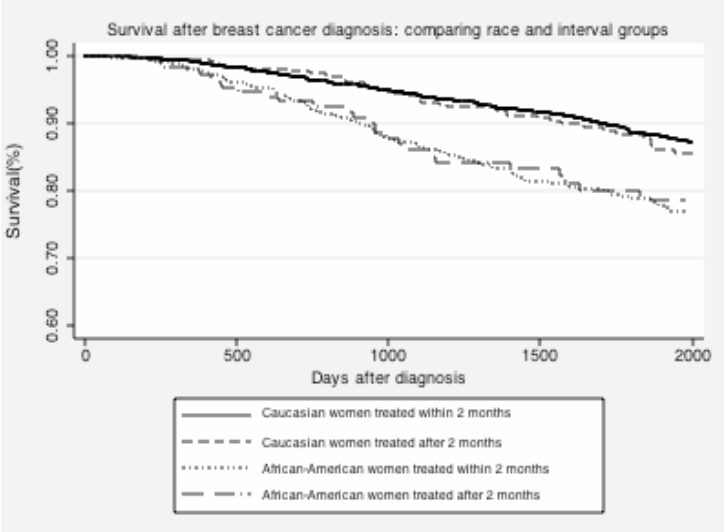

Figure 1

FP01-5

MODIFIED TECHNIQUE OF RADIOTRACER INJECTION FOR THE HIGH VISUALIZATION OF INTERNAL MAMMARY SENTINEL LYMPH NODE IN BREAST DIAGNOSTIC PROCEDURES : PROSPECTIVE STUDY WITH CREDIBLE RESULTS

Yongsheng Wang[1*], **Peng-Fei Qiu**[1], **Yan-Bing Liu**[1], **Guo-Ren Yang**[2]

[1] *Breast Cancer Center, Shandong Cancer Hospital and Institute, China*
[2] *Dept. of Nuclear Medicine, Shandong Cancer Hospital and Institute, China*

Background/Purpose : Even though the 2009 AJCC incorporated the internal mammary sentinel lymph node biopsy (IM-SLNB) concept, there has been limited change in surgeons practice patterns due to the low visualization rate of the internal mammary sentinel lymph nodes (IM-SLNs) with the conventional injection technique (average 13%, range 0-37%). In this prospective study, different radiotracer injection techniques were evaluated to achieve a relative high visualization and detection rate of IM-SLNs (NCT01642511).

Methods : Two hundred patients enrolled in this study were divided into three groups according to the study period and radiotracer (99^{m}Tc-labeled sulfur colloid) injection technique. Group A: conventional technique (radiotracer injection only into the tumor quadrant) for the initial 58 cases; Group B: two-quadrant injection at the 6 and 12 o'clock positions, 2.0~3.0 cm from nipple in the latter 142 cases. Group B was then separated into two groups according to the radiotracer injection volume: Group B1, low volume (<0.5 mL/point, n=41); Group B2, high volume (≥0.5 mL/point, n=101). Radiotracer was injected into the parenchyma under the ultrasonographic guidance for all patients. IM-SLNB was performed for patients with IM-SLNs visualized on preoperative lymphoscintigraphy and/or detected by intraoperative gamma probe.

Results : Group B was associated with a significantly higher IM-SLNs visualization rate (76.1%, 108/142) compared to Group A (15.5%, 9/58, $p<0.001$), and Group B2 with the highest visualization rate (85.1% vs. 53.7% Group B1, $p<0.001$). All techniques had the same visualization rate of the axillary SLNs ($p=0.923$). The visualization rate of IM-SLNs was related to the patient's age ($p=0.032$) and injection volume ($p<0.001$). The successful rate of IM-SLNB was 93.7%, and arrived 100% after 20 cases learning curve. The postoperative IM-SLNB complications were 0.

Conclusion : Modified technique of radiotracer injection (Qiu's injection technique: two-quadrant, high volume and ultrasonographic guidance) significantly improved the visualization rate of IM-SLNs, provided an effective technique to evaluate the status of internal mammary, and would promote research on the IM-SLNB.

FP01-6

INTRAOPERATIVE FROZEN SECTION ANALYSIS FOR MARGINS ASSESSMENT IN BREAST CONSERVING SURGERY

Min Jung Hwang[1], **Young Jae Ryu**[2], **Sun Hyung Shin**[1], **Jin Seong Cho**[2], **Min Ho Park**[1], **Jung Han Yoon**[1]

[1] *Dept. of Endocrine Surgery and General Surgery, Chonnam National Univ. Hwasun Hospital, Korea*
[2] *Dept. of Surgery, Chonnam National Univ. Hwasun Hospital, Korea*

Background/Purpose : Assessment of margins using permanent section analysis is the standard method. However, if the margin is positive, surgical re-excision is necessary to reduce the likelihood of subsequent local recurrence. Therefore, we analyzed records of patients who received breast conserving surgery with intraoperative frozen section.

Methods : A retrospective analysis was done on 1464tumors in 1455 patients with invasive breast cancer treated by breast conserving surgery between July 2004 and June 2012. Breast tumor was excised with 1 cm macroscopic margin and microscopic margins examined by intraoperative frozen section and permanent section.

Results : A total of 218 (14.9%) patients had atypical hyperplasia (AH)(n=65), carcinoma *in situ* (CIS)(n=106) and invasive cancer (IC)(n=44) on the frozen section analysis. 218 patients underwent immediately re-excision. Of these 65patients with AH, final margins on permanent pathology were negative (n=31 , 48%) , atypia (n=17, 26%) , DCIS (n=17, 26%). Of these 106 patients with CIS, 95patients were CIS or IC in permanent section analysis. Of these 47 patients with IC, permanent section analysis reveals negative (n=3), CIS (n=11), IC (n=33)

Conclusion : Intraoperative analysis of margins using frozen section analysis is effective at minimizing the number of additional operation. Therefore, atypia hyperplasia in frozen section analysis need to additional resection at the time of breast surgery.

FP01-7

CLINICAL BENEFITS OF USING NOMOGRAM FOR PREDICTING POSITIVE RESECTION MARGINS IN BREAST CONSERVING SURGERY

Eunshin Lee, Wonshik Han, Hyeong-Gon Moon, Jisun Kim, Min Kyoon Kim, Tae-Kyung Yoo, Jongjin Kim, Jun Woo Lee, Dong-Young Noh*

Dept. of Surgery, College of Medicine, Seoul National Univ., Korea

Background/Purpose : Achieving a clear resection margin in breast conserving surgery (BCS) is an important factor in tumor recurrence in breast cancer. To obtain clear resection margins and reduce re-excision rates, some surgeons obtain intraoperative assessments of the margins of excised specimens, using intraoperative frozen biopsy. But intraoperative frozen biopsy has several problems such as low sensitivity or longer operation time. We have previously reported a nomogram for prediction of positive resection margin by intergraing preoperatively available clinical and pathologic information. The factors were the presence of microcalcification, mammographic density, tumor size discrepancy between magnetic resonance imaging and ultrasonography, and the presence of ductal carcinoma in situ or lobular carcinoma in needle biopsy specimens.

Methods : We conducted a prospective trial to examine the accuracy and clinical benefits of the nomogram in 442 breast cancer patients (nomogram group) who underwent breast conservation surgery between December 2011 and March 2013, and compared the clinical outcome with that of the 253 patients (control group) who underwent breast conservation between January 2011 and October 2011. For nomogram group, the intraoperative frozen section biopsy was omitted for patients with low nomogram scores

Results : Applying our nomogram did not increase the rate of reoperation due to resection margin positivity when compared to the control group (6.56% vs. 4.25%, p=0.22). Additionally, we experienced a significant reduction in operation time by 15 minutes when compared to the control group ($p<0.001$)

Conclusion : our results show that out nomogram for predicting positive resection margin for patients who receive breast conservation surgery can significantly reduce the operation time without increasing the reoperation rate

FP01-8

CLINICOPATHOLOGICAL STUDY OF BREAST MUCINOUS CARCINOMA SUB-CLASSIFICATION

Yuka Asano, Shinichiro Kashiwagi*, Sae Ishihara, Kento Kurata, Satoru Noda, Hidemi Kawajiri, Tsutomu Takashima, Naoyoshi Onoda, Kosei Hirakawa

Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan

Background/Purpose : Mucinous breast carcinoma (MBC), a special type of breast carcinoma, is the second most common cancer after lobular carcinoma, accounting for 1.3-5.4% of all breast cancers. According to the current General Rules for Clinical and Pathological Recording of Breast Cancer, MBC is characterized by the fact that the cancer cells produce mucus, and nests of mucinous cancer cells occupy almost the entire tumor mass. MBC is classified into mixed mucinous breast carcinoma (MMBC) and pure mucinous breast carcinoma (PMBC) based on whether the tumor is with or without a component of invasive ductal carcinoma, respectively. PMBC is subtyped into hypocellular PMBC (PMBC-A) and hypercellular PMBC (PMBC-B).

Methods : Of 1,041 primary breast carcinomas, 42 were diagnosed as MBC, and were subtyped for comparison purposes.

Results : Forty-two of all breast cancers (4.0%) were MBC, and consisted of 15 MMBC, 17 PMBC-A and 10 PMBC-B. The MBC tumors were more often hormone receptor-positive and HER2-negative than non-MBC tumors. Patients with MMBC, PMBC-B or PMBC-A, in this order, had significantly higher recurrence rates than non-MBC cases ($p=0.0319$, log-rank). Among the 42 MBCs, MMBC showed a significantly higher Ki67 labeling index ($p=0.031$) and nuclear grade ($p<0.001$) than PMBC, and these were not correlated with the hormone receptor or HER2 expression. Among the 27 PMBCs, no significant differences in the clinicopathological characteristics were noted between patients with PBMC-A and those with PMBC-B.

Conclusion : In the NCCN guidelines, MBC is also regarded as “a histological type with a favorable prognosis” in a uniform manner, and “treatment for a histological type with a favorable prognosis” is recommended. However, the results of this study suggest that sub-classification-based, individualized therapeutic strategies should be considered.

FP01-9

BODY SIZE AND WEIGHT MANAGEMENT AMONG LONG TERM CANCER SURVIVORS: PERSPECTIVES FROM CLINICAL CARE PROVIDERS

Ann C. Klassen[1*], **Allison Baker**[1], **Kisha Coa**[2], **Katherine Smith**[2]

[1] *Dept. of Community Health and Prevention, Drexel Univ. School of Public Health, U.S.A.*
[2] *Dept. of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, U.S.A.*

Background/Purpose : Purpose: Lifestyle modification to support a healthy weight is a key component of health promotion in cancer survivorship, but little is known about the best ways to support survivors' weight management in clinical settings. To begin to address these gaps, this exploratory study sought to describe how clinical care providers conceptualize and address issues of body size and weight management among cancer survivors.

Methods : Methods: In-depth, semi-structured interviews were conducted with 33 members of the cancer care team in both academic and community settings. Interviews were transcribed and analyzed thematically using qualitative analysis methods.

Results : Results: Provider perspectives on body size and weight management differed based on professional roles and patient populations. Providers conceptualized weight in relation to acute treatment, cancer outcomes, or overall health and comorbidities. These patterns were reflected in their reported framing of weight discussions with survivors, though providers indicated that they counsel patients on weight to varying extents. Providers felt that survivors are motivated to lose weight, particularly due comorbidity concerns, but face numerous barriers to doing so.

Conclusion : Conclusions: Clinicians described a complex array of patient and provider factors influencing survivors' weight management. Differences between various types of providers were especially salient. These findings point to many opportunities for future research and intervention. There is a continued need for evidence-based resources to support survivors' weight management in clinical settings, and various capacity barriers must be addressed. Effective strategies for communicating about survivors' weight management, at both population and interpersonal levels, should be further explored.

FP02-1

IN UTERO EXPOSURE TO DIETARY LIPOTROPES SUPPRESSES CHEMICALLY-INDUCED MAMMARY CARCINOGENESIS

Chung Park[1*], **Kyongshin Cho**[2], **Lawrence Mabasa**[1], **Courtney Anderson**[1], **Sajin Bae**[3], **Dana Walsh**[4]

[1] *Dept. of Animal Sciences, North Dakota State Univ., U.S.A.*
[2] *Dept. of Chemistry and Bio-Chemistry, North Dakota State Univ., U.S.A.*
[3] *Division of Nutritional Sciences, Cornell Univ., U.S.A.*
[4] *School of Medicine, Univ. of North Carolina, U.S.A.*

Background/Purpose : Lipotropes are methyl group containing nutrients (including choline, methionine, folic acid, and vitamin B12) that play key roles in one-carbon metabolism, a process that provides the methyl groups for all biological methylation pathways and is critical in the alteration of gene expression and subsequent growth of cancer cells. Although maternal lipotropes are known to affect offspring's development, their role in the cancer risk of offspring is largely unknown. The purpose of this study was to determine if in utero exposure to maternal high-dose lipotropes has an effect on mammary carcinogenesis.

Methods : Thirty pregnant Sprague-Dawley rats were fed either the control or lipotropes-supplemented diet. The control diet was the AIN-93G semi-purified diet with basal levels of lipotropes. The high-dose lipotropes diet was formulated to provide five times the basal levels of folic acid, choline, and vitamin B12; L-methionine was 1.8 times the basal level to avoid potential toxicity. At parturition, dams were fed the control diet; after weaning, offspring were kept on the control diet until termination of the study. Female offspring from each group were injected with a single dose of N-nitroso-N-methylurea carcinogen during puberty to induce mammary tumors. Animals were monitored for mammary tumor development, and upon detection tumor latency, tumor incidence, tumor multiplicity, tumor volume, and survival rate were recorded. Mammary tumor tissues were analyzed for transcription of genes including, histone deacetylase 1 (Hdac1) and methyl CpG binding protein 2 (Mecp2).

Results : In utero exposure to lipotropes-supplemented diet significantly increased tumor latency by 3 weeks and decreased tumor incidence by 13%, tumor multiplicity by 60%, and tumor volume by 77% as compared to the control diet. Furthermore, the lipotropes diet significantly improved survival rate by 34%. Gene transcription analysis revealed a significant decrease in Hdac1 (0.48 fold decrease) and Mecp2 (0.39 fold decrease) mRNAs in the mammary tumor tissues of offspring exposed to maternal lipotropic diet as compared to their control counterpart.

Conclusion : Our findings provide evidence that in utero exposure to dietary high-dose lipotropes reduces mammary carcinogenesis. The inhibition of mammary carcinogenesis was correlated with a decrease in the expression of Hdac1 and Mecp2 genes, suggesting that maternal methyl diet may induce epigenetic alterations of the expression of genes involved in mammary tumor initiation and development. These results may potentially be used to develop practical maternal dietary strategies that decrease the lifetime risk of breast cancer [Funded by the NIH-National Cancer Institute (1R15CA164768-01A1)].

FP02-2

CASPASE-2 PLAYS A KEY ROLE IN CELL DEATH INDUCTION BY TAXANES IN BREAST CANCER CELLS

Michael Jelinek[1], **Kamila Balusikova**[1], **Vlasta Nemcova- Furstova**[1], **Dana Kopperova**[1], **Jan Sramek**[1], **Ilaria Zanardi**[2], **Iwao Ojima**[3], **Jan Kovar**[1*]

[1] *Dept. of Cell and Molecular Biology, Third Faculty of Medicine, Charles Univ., Czech Republic*
[2] *Institute of Chemical Biology and Drug Discovery, State Univ. of New York at Stony Brook, U.S.A.*
[3] *Dept. of Chemistry, Institute of Chemical Biology and Drug Discovery, State Univ. of New York at Stony Brook, U.S.A.*

Background/Purpose : We studied the role of caspase-2 in apoptosis induction by taxanes (paclitaxel, novel taxane SB-T-1216) in breast cancer cells.

Methods : We employed SK-BR-3 (nonfunctional p53, functional caspase-3) and MCF-7 (functional p53, nonfunctional caspase-3) breast cancer cell lines.

Results : Both taxanes induced apoptosis in SK-BR-3 as well as MCF-7 cells. Caspase-2 activity in SK-BR-3 cells increased approximately 15-fold after the application of both taxanes at the death-inducing concentration (100 nM). In MCF-7 cells, caspase-2 activity increased approximately 11-fold after the application of taxanes (300 nM). Caspase-2 activation was confirmed by decreasing levels of procaspase-2, increasing levels of cleaved caspase-2 and the cleavage of caspase-2 substrate golgin-160. The inhibition of caspase-2 expression using siRNA increased the number of surviving cells more than 2-fold in MCF-7 cells, and at least 4-fold in SK-BR-3 cells, after the application of death-inducing concentration of taxanes. The inhibition of caspase-2 expression also resulted in decreased activation of initiator caspases (caspase-8, caspase-9) as well as executioner caspases (caspase-3, caspase-7) in both cell lines after the application of taxanes. In control cells, caspase-2 seemed to be mainly localized in the nucleus. After the application of taxanes, it was released from the nucleus to the cytosol, due to the long-term disintegration of the nuclear envelope, in both cell lines. Taxane application led to some formation of PIDDosome complex in both cell lines. After taxane application, p21WAF1/CIP1 expression was only induced in MCF-7 cells with functional p53. However, taxane application did not result in a significant increase of PIDD expression in either SK-BR-3 or MCF-7 cells. The inhibition of RAIDD expression using siRNA did not affect the number of surviving SK-BR-3 and MCF-7 cells after taxane application at all.

Conclusion : Caspase-2 is required for apoptosis induction by taxanes in breast cancer cells. We suggest that caspase-2 plays the role of an apical caspase in these cells. Caspase-2 seems to be activated via other mechanism than PIDDosome formation. It follows the release of caspase-2 from the nucleus to the cytosol. This work was supported by grant 301/09/0362 from the Grant Agency of the Czech Republic and by grant CA 103314 from the National Cancer Institute, USA.

FP02-3

MET IS A POTENTIAL TARGET FOR USE IN COMBINATION THERAPY WITH EGFR INHIBITION IN TRIPLE-NEGATIVE/BASAL-LIKE BREAST CANCER

Yu Jin Kim[1], **Jong-Sun Choi**[2], **Ji-Young Song**[3], **Yoon-La Choi**[4*]

[1] *Laboratory of Cancer Genomics and Molecular Pathology, Samsung Biomedical Research Institute, Samsung Medical Center, Korea*

[2] *Dept. of Pathology, Dongguk Univ., Ilsan Hospital, Korea*

[3] *Institute for Refractory Cancer Research, Samsung Medical Center, Korea*

[4] *Dept. of Pathology, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : MET, a cell surface receptor for hepatocyte growth factor, has been known to be involved in the development of TNBC/BLBC (Triple-Negative Breast Cancer/Basal-Like Subtype). However, its utility as therapeutic target in this subtype of breast cancer is poorly understood. To fully evaluate MET as a potential therapeutic target for TNBC/BLBC, we investigated the relationship between MET expression and clinical outcomes of patients with breast cancer and the functional effect of MET inhibition.

Methods : We investigated the association of MET expression with clinical outcomes of patients with several types of breast cancer and further assessed the effect of anti-MET therapy in TNBC cell lines, which show the relatively high expression of MET.

Results : By using automated immunohistochemistry (Ventana, USA), we analysed the expression of MET in 924 breast cancer patients with relevant clinicopathologic parameters. BLBC showed the strongest relationship with MET expression (57.5%, P<0.001). High expression of MET in these subtypes resulted in poor overall survival (OS)(P=0.001) and disease-free survival (DFS)(P=0.010). MET expression was relatively high in TNBC cell lines, and silencing of MET via siRNA reduced cell proliferation and migration. We observed reduced TNBC cell viability after treatment with the MET inhibitor, PHA-665752. In the most drug-resistant cell line, MDA-MB-468, which showed elevated epidermal growth factor receptor (EGFR) expression, silencing of EGFR resulted in increased sensitivity to PHA-665752 treatment. We confirmed that PHA-665752 synergizes with the EGFR inhibitor erlotinib to decrease the viability of MDA-MB-468 cells. TNBC patients co-expressing MET and EGFR showed significantly worse DFS than patients expressing EGFR alone (P=0.021).

Conclusion : Our findings strongly suggest that MET may be a therapeutic target in TNBC and that the combined therapy of MET and EGFR may be beneficial for the treatment of TNBC/BLBC patients.

FP02-4

HISTONE DEACETYLASES INHIBITOR SAHA ENHANCES ANTI-TUMOR EFFECTS OF POLY (ADP-RIBOSE) POLYMERASE INHIBITOR OLAPARIB IN TRIPLE-NEGATIVE BREAST CANCER CELLS

Ahrum Min, Seock-Ah Im*, Hyemin Jang, Kyung-Hun Lee, Tae-Yong Kim, Sae-Won Han, Do-Youn Oh, Tae-You Kim, Yung-Jue Bang

Cancer Research Institute, College of Medicine, Seoul National Univ., Korea

Background/Purpose : The poly (ADP-ribose) polymerase (PARP) inhibitor, olaparib, has been found to have a therapeutic potential for treating cancers that have an impaired DNA repair ability. However, some cancer presents acquired resistance to PARP inhibitor or platinum and PARP inhibitor combinational treatment. Histone deacetylases (HDACs) are important to enable functional homologous recombination (HR) by regulating the expression of HR-related genes and promoting the accurate assembly of HR-directed subnuclear foci. Thus, HDAC inhibitors have emerged recently as a class of therapeutic agents for the treatment of cancer by inhibiting DNA repair. For this mechanism, HDAC inhibition would enhance the anti-tumor effect of PARP inhibitor in cancer cells by blocking DNA repair pathway.

Methods : We determined whether SAHA, a HDAC inhibitor could enhance the growth inhibition of olaparib on breast cancer cell lines using MTT assay. We examined whether exposure to SAHA affects the expression level of genes involved in HR. The accumulation of DNA double strand breaks (DSBs) induced by combination treatment was accessed by the comet assay. Cell cycle analysis and molecular changes induced by combination of olaparib plus SAHA were also performed. These in vitro data were validated in the in vivo xenograft model as well.

Results : Triple-negative breast cancer cell lines showed heterogeneous response to dual inhibition of PARP and HDACs. SAHA enhanced olaparib-induced cell death of MDA-MB-157 and HCC1143 but not of HCC70 and MDA-MB-468. Combination of SAHA plus olaparib caused a greater decrease of pAKT, pERK, and pSTAT3 in MDA-MB-157 and HCC1143 cells than monotherapy either SAHA or olaparib. There was no change in proliferative pathway activation in HCC70 and MDA-MB-468 cells. Furthermore, inhibition of PARP increased the accumulation of DNA DSBs induced by SAHA in only two cell lines, MDA-MB-157 and HCC1143. Our findings showed that triple-negative breast cancer cells are differentially effective to combination of SAHA plus olaparib which increased levels of unrepaired DNA DSBs.

Conclusion : Olaparib showed enhanced growth inhibitory activity against several triple-negative breast cancer cells with HDAC inhibitor, SAHA. The combination of SAHA plus olaparib induced accumulation of DNA DSBs and also down-regulated signal transduction. Our results provide a rationale for the future clinical trials of olaparib combined with SAHA in the treatment of cancers that have an impaired DNA repair ability.

FP02-5

TARGETING MnSOD IN BASAL BREAST CARCINOMA USING AGONISTS OF PPARγ: A NEW STRATEGY FOR ENHANCING CHEMOSENSITIVITY

Ser Yue Loo[1], **Alan Prem Kumar**[2], **Shazib Pervaiz**[3], **Marie Veronique Clement**[4*]

[1] *Dept. of Biochemistry, National Univ. of Singapore, Singapore*
[2] *Dept. of Pharmacology, Cancer Science Institute, National Univ. of Singapore, Singapore*
[3] *Dept. of Physiology, NUS Graduate School for Integrative Sciences and Engineering, National Univ. of Singapore, Singapore*
[4] *Dept. of Biochemistry, NUS Graduate School for Integrative Sciences and Engineering, National Univ. of Singapore, Singapore*

Background/Purpose : While a considerable progress has been made in the diagnosis and treatment of estrogen-dependent breast cancer, the estrogen-independent breast cancer, particularly the basal subtype tumors, are associated with poor prognosis due to a lack of target-specific therapeutic options. Recent evidence indicates increased expression of Manganese superoxide dismutase (MnSOD), a major redox regulator, in a variety of human cancers. We hypothesize that increased MnSOD expression in aggressive breast cancers could be an attractive target for enhancing chemosensitivity.

Methods : Based on data from two microarray platforms, MnSOD expression was compared across several subtypes of breast cancer. Kaplan-Meier analysis was performed to compare survival rates between patients with high and low MnSOD expressions. Knockdown of MnSOD was performed to sensitize basal-like cell lines to drug-induced apoptosis. Based on recent findings that MnSOD is a target gene of peroxisome proliferator-activated receptor gamma (PPARγ), we employed PPARγ activation via endogenous ligand 15d-PGJ2 and synthetic glitazones to repress MnSOD expression and enhance chemosensitivity in basal-like cell lines.

Results : MnSOD expression was significantly amplified in the basal-subtype of human breast cancer, a highly aggressive tumor with limited treatment options. A similar expression pattern was observed in the basal-like cell lines, MDA-MB-231 and BT549, compared to the luminal MCF-7 and T47D cells. Knockdown of MnSOD sensitized basal-like cell lines to drug-induced apoptosis, while drug resistance was associated with significantly increased MnSOD expression. PPARγ activation significantly reduced MnSOD expression, increased chemosensitivity and inhibited tumor growth in the basal-like cell line. Furthermore, MnSOD expression was significantly reduced in clinical tissues derived from breast cancer patients who had received synthetic ligands of PPARγ as anti-diabetic therapy. Finally, mitochondrial ROS upon MnSOD repression was critical in the chemosensitization of basal-like cell lines, thus demonstrating “oxidative stress therapy” as an antitumor strategy.

Conclusion : These data provide evidence to link increased MnSOD expression with the aggressive basal subtype of breast cancer, and underscore the judicious use of PPARγ ligands for specifically downregulating MnSOD to induce mitochondrial oxidative stress-dependent increase in chemosensitivity of this sub-type of breast cancer.

FP02-6

EXTENSIVE NOVEL HYBRID ISOFORMS REVEALED BY RNA SEQUENCING OF 120 PRIMARY BREAST CANCER SAMPLES

Jisun Kim[1], Hwan-Suk Lee[2], Yong-Ho In[3], Hyeong-Gon Moon[4], Min-Ju Lee[5], Jehwan Park[6], Jung Hoon Woo[7], Seh-Whan Kim[2], Dong-Young Noh[4], Sunghoon Kim[3], Wonshik Han[4*]

[1] *Dept. of Breast Endocrine, Seoul National Univ. Hospital, Korea*
[2] *Macrogen Inc., Korea*
[3] *Bioconvergence Research Center, Korea*
[4] *Dept. of Surgery, Seoul National Univ. Hospital, Korea*
[5] *Cancer Research Institute, College of Medicine, Seoul National Univ., Korea*
[6] *Geference Inc., Korea*
[7] *Dept. of Biomedical Informatics, Columbia Univ. Medical Center, U.S.A.*

Background/Purpose : Recent studies of next generation sequencing (NGS) have highlighted the extensive transcriptional heterogeneity of cancer cells. Alternative splicing is one of the evolutionary process by which cells and tissues achieve their specificity within central dogma. Also it is highly assumed to contribute to oncogenesis and thought to be a critical mechanism how cancer cells gain resistance to therapeutic agents and adapt to various circumstances. Relevance of differential splicing in breast cancer biology is mostly unknown. We performed whole transcriptome sequencing (RNA-Seq) to reveal novel splicing alterations among 120 primary breast cancer samples

Methods : Total RNA was prepared using the Illumina TrueSeq™ RNA sample Preparation Kit and TrueSeq mRNA library was constructed. Clustering and sequencing was done using Illumina HiSeq 2000. RNA-Seq reads were aligned to human reference genome (hg19) using TopHat software and expression was measured using cufflinks software. We used tissues extracted from previously collected 120 fresh-frozen primary breast cancer samples obtained after surgical resection whose clinicopathological data are available. Patients undergone neoadjuvant systemic therapies or stage IV disease at diagnosis were excluded. Thirty-six (30%) cases occurred distant metastasis during follow up. Hormone receptor was positive in 61 (50.8%) samples, 20 (16.7%) had HER2 oncogene overexpression and 36 (30%) were triple negative breast cancer

Results : Total 11345 novel isoforms were detected among 120 tumors. Isoforms of pseudo-genes and exon skipping of the 'non-coding exon' were excluded. Splice variants detected in normal reference were sorted out as well. 4045 were in-frame exon skipping and 4960 were off-frame exon skipping which may lead to protein truncation. 5036 were private exon skipping and 3969 isoforms were detected recurrently in more than 2 samples. To minimize false positivity we confined 'exon skipping' analysis to those with the expression level (Fragments per kilo-base of exon per million fragments mapped, FPKM) of the skipped exon below 0.1 compared to the adjacent exons. Mean number of exon skipping events per sample was 196.8 (range 75-299, SD 35.9). There were no differences in numbers of exon skipping event among breast cancer subtypes nor distant metastasis. We have identified novel exon skipping in ESR1, CHEK2, EIF3E, FGFR, MAP2K, PIK3R2, TERT, VAV3 genes which is strongly suspected to be novel driver isoforms and is under validation process.

Conclusion：We performed whole-transcriptome sequencing with a large set of primary breast cancer samples and revealed extensive transcriptional heterogeneity by isoform profiling. As distinguishing the natural transcriptomic dynamics from oncogenic 'driver' isoform is a major challenge, validation and functional studies are ongoing.

FP02-7

REDUCTION OF BREAST CANCER RELAPSES WITH PERIOPERATIVE NON-STEROIDAL ANTI-INFLAMMATORY DRUGS: PERHAPS TRANSIENT SYSTEMIC INFLAMMATION POST SURGERY PRECIPITATES METASTATIC ACTIVITY

Michael Retsky

Dept. of Environmental Health, Harvard School of Public Health, U.S.A.

Background/Purpose：While there have been important improvements in recent years, a general method to prevent relapses from early stage cancer is one of the most important unsolved problems in oncology. My colleagues and I have been studying an unexpected bimodal pattern of hazard of relapse among early stage breast cancer patients that has been identified in multiple databases from USA, Europe and Asia. We have proposed that late relapses result from steady stochastic progressions from single dormant malignant cells to avascular micrometastases and then on to growing deposits. However in order to explain early relapses, we had to postulate that something happens at about the time of surgery to provoke sudden exits from dormant phases to active growth and then to detection. Most relapses in breast cancer are in the early category.

Methods：We have been studying clinical and experimental data in an attempt to understand this process and how it may be prevented. We report what may be an important development.

Results：Recent data from Forget et al. suggests an unexpected mechanism. They retrospectively examined results from 327 consecutive breast cancer patients comparing various perioperative analgesics and anesthetics in one Belgian hospital and one surgeon. Patients were treated with mastectomy and conventional adjuvant therapy. A common non-steroidal anti-inflammatory drug (NSAID) analgesic used in surgery produced far superior disease-free survival in the first 5 years after surgery. The expected prominent early relapse events in months 9-18 are reduced 5-fold. Other investigators report inflammatory markers are elevated in serum for 1-2 weeks post primary surgery.

Conclusion：If these observations hold up to further scrutiny, it could mean that the simple use of a safe, inexpensive and effective anti-inflammatory agent at surgery might dramatically reduce early relapses. Transient systemic inflammation accompanying surgery could facilitate angiogenesis of dormant micrometastases, proliferation of dormant single cells, and seeding of circulating cancer stem cells (perhaps released from bone marrow as part of the wound healing process) resulting in early relapse and could have been effectively blocked by the perioperative anti-inflammatory agent.

FP02-8

INFLUENCE OF CD44 GENE POLYMORPHISMS IN BREAST CANCER PROGNOSIS

Sonam Tulsyan

Dept. of Genetics, Sanjay Gandhi Postgraduate Institute of Medical Science, India

Background/Purpose : CD44, a cell surface marker plays a significant role in breast cancer cell growth, differentiation, invasion, angiogenesis and tumor metastasis. Therefore, we aimed to evaluate the influence of CD44 gene polymorphisms in breast cancer prediction and prognosis in North Indian population.

Methods : A total of 258 breast cancer females and 131 healthy controls were included in the case-control study for risk prediction. According to RECIST, 114 patients who received neo-adjuvant chemotherapy were recruited for the evaluation of breast cancer prognosis. We examined the association of tagging SNP (rs353639) of Hapmap Gujrati Indians in Houston (GIH population) in CD44 gene along with a significant reported SNP (rs13347) in Chinese population by genotyping using Taqman allelic discrimination assays. Statistical analysis was done using SPSS software, version 17. In-silico analysis for prediction of functional effects was done using F-SNP and FAST-SNP.

Results : On performing univariate analysis with clinicopathological characteristics and treatment response, we found significant association of genotype (CT+TT) of rs13347 polymorphism with earlier age of onset (P=0.029). However, significance was lost in multivariate analysis. For rs353639 polymorphism, significant association was seen with clinical tumour size, both at the genotypic (AC+CC) (p=0.039) as well as the allelic (C) (p=0.042) levels. On performing multivariate analysis, increased significance of variant genotype (p=0.017, OR=4.29) and allele (p=0.025) of rs353639 was found with clinical tumour size. In-silico analysis using F-SNP, showed altered transcriptional regulation for rs353639 polymorphism.

Conclusion : CD44 rs353639 genetic variants may have significant effect in breast cancer prognosis. However, both the polymorphisms- rs13347 and rs353639 had no effect on breast cancer susceptibility.

FP02-9

PROGNOSTIC IMPACT OF YB-1 IN BREAST CANCER

Anbok Lee[1], **Heejung Park**[2], **Juhyun Woo**[1], **Cholhee Yun**[1], **Sun Young Min**[1], **Yunsuk Kim**[1], **Seungwon Yu**[1], **Sunhee Sung**[2], **Woosung Lim**[1], **Namsun Paik**[1], **Byung-In Moon**[1*]

[1] *Dept. of Surgery, Ewha Womans Univ. Hospital, Korea*
[2] *Dept. of Pathology, Ewha Womans Univ. Hospital, Korea*

Background/Purpose : The human Y-box binding protein 1 (YB-1) is a member of the DNA/RNA-binding family of proteins and regulates transcription and translation of genes. Several studies suggested oncogenic role of YB-1 in various cancers. So we performed this study to evaluate YB-1 as a value for prognostic factor in breast cancer.

Methods : Among the patients who underwent curative surgery between Jan. 2003 and Dec.2008, 231 patients were included in this study. All specimens of these patients were fixed in formalin, embedded in paraffin, and stored at the pathology archive in our hospital. Immunohistochemical staining was performed using this block. Patients were divided to two groups according to nuclear expression of YB-1 in tumor cell (positive versus negative).The relationship between nuclear expression of YB-1 and clinicopathological characteristics were analyzed. The prognosis according to nuclear expression of YB-1 was also assessed.

Results : Negative estrogen and progesterone receptor, high histologic and nuclear grade, and high Ki67 were related with positive expression of YB-1 in nucleus ($p<0.05$). No significant difference was observed in relapse free survival between two groups ($p=0.744$), however, there was a significant difference in overall survival (OS) ($p=0.036$). In multivariate analysis for OS, YB-1 was an independent prognostic factor ($p=0.030$).

Conclusion : Nuclear expression of YB-1 in tumor cell is an independent prognostic factor for breast cancer and related with poor prognostic factors.

FP03-1

NO FURTHER AXILLARY DISSECTION IN SENTINEL LYMPH NODE-NEGATIVE BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH INITIAL CYTOLOGICALLY-PROVEN AXILLARY NODE METASTASIS

Min Kuk Kim, Hyun Chul Lee, Jun Ho Lee, Jiyoung Kim, Soo Youn Bae, Se Kyung Lee, Sangmin Kim, Won Ho Kil, Seouk Won Kim, Seok Jin Nam, Jung Eon Lee*

Dept. of Surgery, Samsung Medical Center, Korea

Background/Purpose : In patients with fine needle aspiration (FNA)-proven axillary lymph node metastasis at diagnosis (cN+), the current standard surgical procedure is axillary lymph node dissection (ALND) at definitive surgery after neoadjuvant chemotherapy (NAC). However, growing evidences suggest that SLNB after NAC is feasible and may demonstrate acceptable performance in selected patients. We performed sentinel lymph node biopsy in patients treated with cytologically-confirmed axillary lymph nodes metastases at presentation, who converted to a clinically negative axillary status after NAC (ycN0).

Methods : We retrospectively evaluated 240 patients with invasive breast cancer with ultrasound-guided FNA-proven axillary nodal metastases at the time of diagnosis. All patients received NAC and underwent surgery at Samsung medical center between October 2007 and May 2013. Among these patients, 75 patients underwent SLNB. These patients converted to clinically node-negative disease (ycN0) after NAC on breast MRI or PET/CT scan. A combined detection technique was used with radioisotope and blue dye for the detection of SLN. Patients with negative SLN on frozen pathology and low clinical suspicion of metastasis during operation were not performed further ALND.

Results : The detection rate of SLNB was 93.3 % (70/75), and median number of retrieved sentinel lymph nodes was 3.0 (range 1-8). False negative rate was 6.7 % (1/15). Of these 75 patients, 35 (46.6 %) patients had positive sentinel lymph nodes (ypN+) and underwent ALND. Thirty-five (46.6 %) patients had tumor-free sentinel lymph nodes (ypN0sn) and 20 patients of them were followed without subsequent ALND. In these SLN-negative patients without further ALND, 9 patients were HER2-enriched subtypes and 9 patients, TNBC subtypes. Only two of them were Luminal B subtypes. The median follow-up period was 12.0 months (range 0-26 months) with 2 events; 1 regional recurrence in ipsilateral supraclavicular node and 1 systemic recurrence in brain on postoperative 7 months and 5 months, respectively. There has not occurred an ipsilateral axillary recurrence so far.

Conclusion : Although the follow-up was not long enough to conclude, this study tried to demonstrate that SLNB after NAC was feasible and further ALND may not be necessary in patients with SLN-negative disease (ypN0sn).

FP03-2

ROLE OF AXILLARY CLEARANCE WITH TUMOR POSITIVE SENTINEL NODE IN MASTECTOMY GROUP: IS THE RESULTS OF ACOSOG Z0011 TRIAL ADAPTABLE TO MASTECTOMY PATIENT?

Ji Young You[1], Eun Jin Song[1], Moo Hyun Lee[1], So-Youn Jung[1], See Youn Lee[1], Han Sung Kang[1], Jung Sil Ro[2], Eun Sook Lee[1*]

[1] Dept. of Surgery, Center for Breast Cancer, National Cancer Center, Korea

[2] Dept. of Medical Oncology, Center for Breast Cancer, National Cancer Center, Korea

Background/Purpose : Recent data from ACOSOG Z0011 trial or AMAROS trial suggest that axillary lymph node dissection (ALND) may be unnecessary for patients with positive sentinel lymph node biopsy (SLNB) receiving breast conserving surgery (BCS) with irradiation. However, consensus statements and guidelines until recently recommended that patients with mastectomy and tumor positive sentinel node undergo completion ALND. In this preliminary study, we compared these patients who did not undergo ALND with two other groups, which patients received BCS and irradiation with SLNB only and received mastectomy with ALND. We analyzed the loco-regional recurrence rate to show no differences of outcomes among three groups.

Methods : We identified 6,163 women with invasive breast cancer who underwent surgical resection at the National Cancer Center (Goyang,Gyeonggi-do,Korea) between January 2000 to December 2011. Clinicopathological data obtained from prospective collecting medical database of our institution were analyzed retrospectively. Among the patients with node positive on sentinel biopsy, the mastectomy with SLNB only was performed in 39 cases, mastectomy with ALND in 181 cases and BCS with SLNB and irradiation in 165 cases. The primary end point was loco-regional recurrence rate.

Results : Clinical and tumor characteristics were similar between each group. The mean tumor size was 3.1 cm with mastectomy with SLNB group, 3.0cm with mastectomy with ALND group and 2.0cm with BCS group. The median number of nodes removed in both SLNB groups was 3.2. There was not a single case of loco-regional recurrence in sentinel groups. At a median follow-up of 61.0 months (last follow-up, May 2013), the locoregional recurrence rate of each group were 0% in BCS with SLNB and mastectomy with SLNB only and 1.7% in mastectomy with ALND (p=0.182).

Conclusion : In our study, there was no difference in loco-regional recurrence rate as above. This results lend weight to the argument that SLNB without ALND may be reasonable management for selected patients with appropriate surgery and adjuvant systemic therapy. This study can be regarded as a preliminary study with a sufficient value because we have performed treatment with relatively consistent policy at a single institution. In order to be made consensus, the large volume of prospective randomized clinical trial with accurate protocol will be needed.

FP03-3

REAL-TIME 3D VIRTUAL NAVIGATION - IT AND BREAST SURGERY -

Masato Suzuki, Keiji Koda, Masato Yamazaki, Kiyohiko Shuto, Chihiro Kosugi, Atsushi Hirano, Risa Shiragami, Hidehito Arimitsu

Dept. of Surgery, Teikyo Univ. Chiba Medical Center, Japan

Background/Purpose : Information technology (IT) has been playing an important role in the medical field. Electronic ordering system and PACS (picture archiving and communication system) are widely adopted in many hospitals. It is not overstatement that we cannot perform medical treatment without IT. In general, patients with early stage breast cancer undergo primary surgery, and many of them are the candidates of sentinel lymph node biopsy (SLNB). For patients who desire breast conserving therapy (BCT) but are not candidates at the time of presentation, an alternative approach is the use of primary systemic therapy (PST). After PST, sometimes it is difficult to determine the appropriate resection-line at the time of surgical operation because of tumor size reduction or indistinct boundary of the tumor. For the improvement of success rate and safety, we developed a new navigation technique using information technology (IT) and ubiquitous computing system.

Methods : Multi-detector row computed tomography (MD-CT) has been performed for all breast cancer patients in our institute. CT lymphograhy (CT-LG) with iopamidol was indicated for the SLNB candidate. DICOM (The Digital Imaging and Communications in Medicine) images of MD-CT were analyzed by image processing software 'OsiriX'. OsiriX is an open source software (http://www.osirix-viewer.com) which has been specifically designed for navigation and visualization of multimodality and multidimensional images. At the time of surgery, 3 dimensional (3D) volume rendering images were superimposed directly on the patients' skin from projector which was connected to a personal computer in the operating room. CT-LG data were used for SLND and pre-PST data were used for BCT after PST.

Results : 'Less invasive' surgical operations are performed with small wound, so it is getting more difficult for residents and trainee to understand the 3D anatomy from narrow view area. 3D reconstruction MD-CT images were helpful to understand the anatomy and to perform pre-operative simulation. We could see 'real-time' rendering images (from skin to organ by layer to layer) on the patient's body. By using 3D imaging data of CT-LG, we could recognize precise SLN location and by using pre-PST imaging data, we could decide suitable resection-line easier than before.

Conclusion : This new technique does not need some expensive equipments and easily performed by surgeon. All we need is an ordinary personal computer and projector. Ubiquitous computing system such as tablet PC or iPod using 'cloud' can make more comfortable environment.

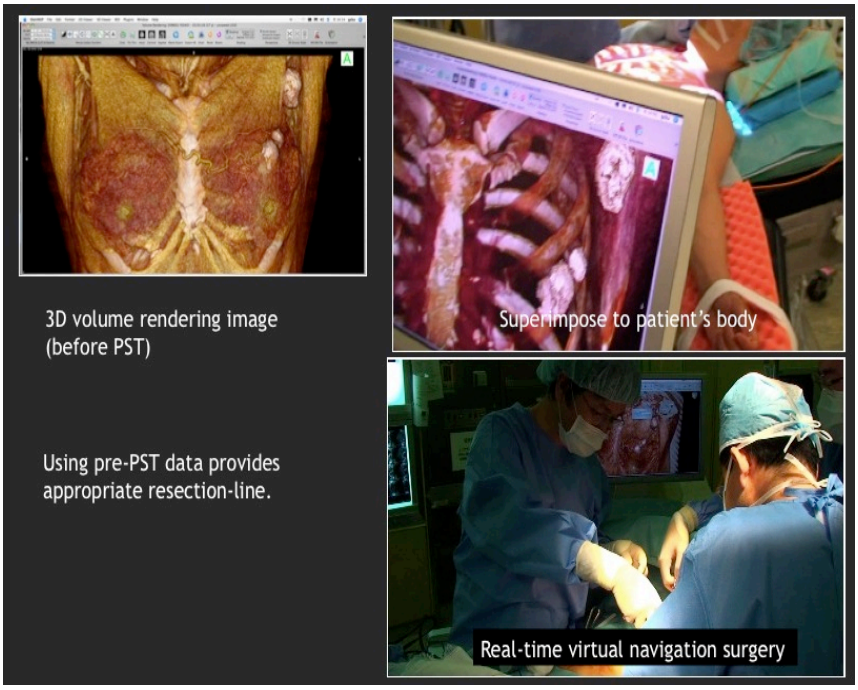

Figure 1

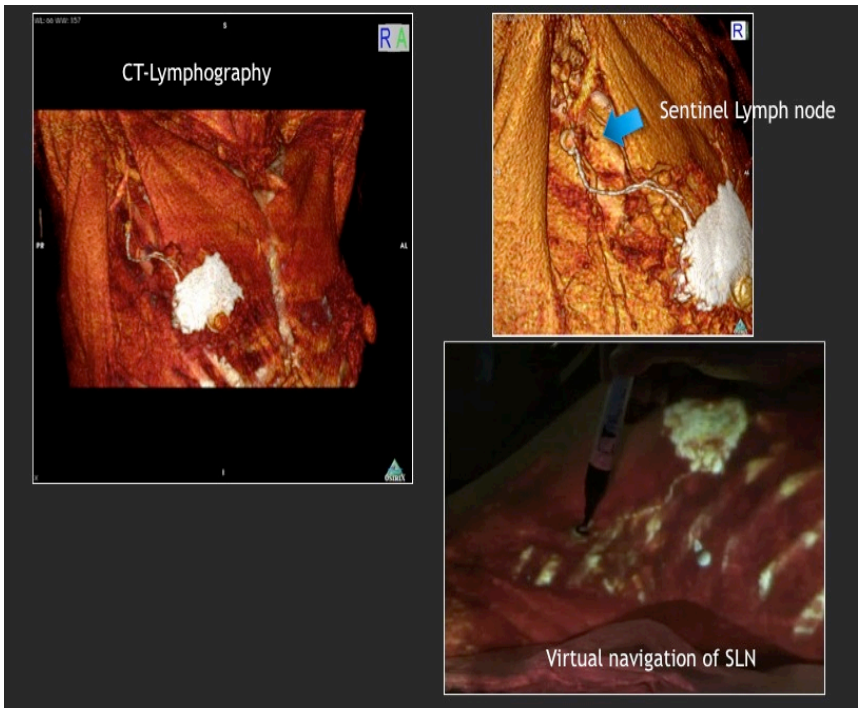

Figure 2

FP03-4

NEOADJUVANT CHEMOTHERAPY IN YOUNG AGE BREAST CANCER: SURVIVAL BENEFIT OVER ADJUVANT CHEMOTHERAPY IN CLINICALLY T2 NODE POSITIVE PATIENTS

Min Kyoon Kim, Hyeong-Gon Moon, Jisun Kim, Jun Woo Lee, Tae-Kyung Yoo, Jongjin Kim, Eunshin Lee, Dong-Young Noh, Wonshik Han*

Dept. of Surgery, Seoul National Univ. Hospital, Korea

Background/Purpose : The downstaging of the primary tumor and the increase in breast conservation rates seems to be the only clinical benefit of neoadjuvant systemic therapy(NST) in breast cancer treatment, given that several studies failed to demonstrate an improvement of overall survival compared with postoperative adjuvant chemotherapy. In Europe, S6 trial showed better early outcome in survival in favour of the neoadjuvant chemotherapy group compared to adjuvant chemotherapy group in premenopausal patients without significantly modifying long-term event rates. The aim of this study was to assess a potential advantage in survival by neoadjuvant as compared to adjuvant chemotherapy in young age breast cancer patients.

Methods : Between January 2001 and December 2008, 1169 consecutive patients with breast cancer aged under 40 underwent adjuvant chemotherapy before or after surgery. Prospectively collected medical records for all patients were reviewed retrospectively. For the comparison of survival between neoadjuvant versus adjuvant chemotherapy group, clinically T2 and node positive patients were retrieved. Survival curves were derived from Kaplan-Meier estimates and compared by log-rank test.

Results : Of the 1169 patients, 203 (17.3%) patients were treated with neoadjuvant chemotherapy, and they were grouped as 'NST' and 'non-NST' according to initial treatment. About 47% patients in each group were clinically T2 patients (99[47.8%] in NST group, 453 [46.9%] in non-NST group). Among them, clinically T2 and node positive patients were 188, 97 patients in NST group, 91 patients in non-NST group each. The median age was 35.11±3.9 years old and HER2 amplification was observed as 23.5%, and they were not different between two groups ($p=0.146$ and 0.941 each) Significant lower hormone receptor expression rate and higher Ki-67 level were observed in NST group ($p=0.03$ and <0.0001, respectively) Breast conservation surgery rate was also significantly different between two groups, more favorable results in NST group (67% in NST group and 37.4% in non-NST group, $p<0.0001$). During median follow-up period of 61 months (range 44 - 148 months), we observed a statistically significant difference ($p=0.011$) in survival in favour of the NST group. This benefit of survival was presented consistently regardless of hormone receptor expression. A similar trend was seen when the time to distant disease recurrence was evaluated ($p=0.176$). And this trend was more prominent in hormone receptor negative patients, but still not statistically significant. ($p=0.144$) The mean total dose of chemotherapy administered was similar in both groups. Improved survival figures in the NST group could be the result of the early initiation of systemic treatment, but the trend in favour of decreased metastases was not statistically significant.

Conclusion : A potential advantage of primary over adjuvant chemotherapy in young age breast cancer patients' survival might be proposed by this results.

FP03-5

BREAST CANCER 2013: TIME TO ACKNOWLEDGE MEDICAL THERAPY FIRST

Maria Antonia Coccia-Portugal[1], **Adriaan Jacobs**[2], **Maria M Ribeiro**[3]

[1] *Dept. of Medical Oncology, Eastleigh Breast Care Centre, South Africa*
[2] *Dept. of Surgery, Eastleigh Breast Care Centre, South Africa*
[3] *Dept. of Oncology, Eastleigh Breast Care Centre, South Africa*

Background/Purpose

Breast Cancer treatment has traditionally been in the domain of surgery. Mastectomy was the cornerstone and standard of care until medical treatment became available. A seventy-year period of local treatment alone made no overall impact, survival improving only since early introduction of medical therapy. Tumour Biology now supersedes anatomical staging as the prime foundation determinant for medical treatment decision.

Methods : Time to treat the disease at diagnosis:

The core biopsy is mandatory to identify the tumour biology (Grade, Hormonal Receptors, HER2 / neu, Ki-67, others). Early referral of patients for multidisciplinary team evaluation and planning is essential. The treatment must be guided by the tumour biological characteristics (Chemotherapy/Hormonal). All Breast Cancers need to be treated medically; excepting small tumours (< 1 cm) without therapeutical targets (triple negative). NSABP B18 study confirmed that preoperative chemotherapy is as effective as postoperative chemotherapy in the outcome of women with operable breast cancer.

Results : Advantages motivating systemic medical therapy before surgery:

Targeting potential micro spreading at diagnosis in high risk disease without disturbance of tumor angiogenesis; Enabling the oncologist to check response to medical treatment; and, if poor, to change with a possible survival benefit; Avoiding toxicity of ineffective medical therapy, as treatment given after tumor excision is blind therapy; Facilitating surgical excision with clear margins; Achieving a better cosmetic result and a more motivated patient; Pathological reevaluation post surgery will show the final efficacy of the given treatment and the identification of resistant clones; Thereafter plan and adjust further therapy.

Conclusion: Recommendation for a change in the International (consensus) guidelines. Knowledge acquired over the last decades confirmed improved survival with the introduction of medical therapy. It is now time to acknowledge the need to treat the disease medically first, before the surgical management.

FP03-6

EARLY FAILURE OF LOCALLY ADVANCED BREAST CANCERS TO NEOADJUVANT CHEMOTHERAPY: IDENTIFYING THE PATIENTS WHO DO NOT HAVE BENEFIT FROM NEOADJUVANT CHEMOTHERAPY

Moon Ki Choi[1], **Yeon Hee Park**[1], **Jung Yong Hong**[1], **Hyun Ae Jung**[1], **Seok Won Kim**[2], **Won Ho Kil**[2], **Jeong Eon Lee**[2], **Seok Jin Nam**[2], **Jin Seok Ahn**[1], **Young-Hyuck Im**[1*]

[1] *Division of Hematology-Oncology, Dept. of Medicine, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

[2] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : Locally advanced breast cancer (LABC) is a heterogeneous group of diseases. Neoadjuvant chemotherapy (NAC) has been widely used for patients with over the last few decades in order to decrease the extent of the primary tumor, leading to a higher chance for breast conserving surgery, and to improve overall survival by eradicating micrometastatic disease. The goal of this study was to determine predictors of early tumor progression after NAC with the ultimate aim of identifying patients who might benefit from a screening program, or from more aggressive treatment and preventive strategies.

Methods : This study is a retrospective single-center study. Patients who had LABC were included in this analysis from Jan 2005 to Dec 2011 at Samsung Medical Center. Among 404 patients who received NAC, seven patients with distant metastatic disease were excluded. Then number of our final cohort was 397. The clinicopathologic characteristics and disease courses of the patients whose disease progressed within 1 year since NAC had been conducted were analysed.

Results : After NAC, 53 patients (13.4%) had complete response (CR), 250 (62.8%) had partial response (PR), 83 (20.9%) had stable disease (SD), 9 (2.3%) had progressive disease (PD), and 2 (0.5%) were not evaluable. Thirty-eight of 397 patients (9.6%) were progressed within 1 year after NAC was performed during median follow-up period of 35.7 months. Of the 38 patients, clinical response after NAC was evaluated as a CR for 3 patients, a PR for 19 patients, a SD for 10 patients, and as a PD for 6 patients. Pathologic complete remission was found in two patients (5.3%, 2/38). The number of HER2+ve irrespective of HR status and triple negative breast cancer (TNBC) patients were 13 (34.2%) and 17 (44.7%), respectively. CNS was the most common site of first distant metastasis (31.6%, 12/38). Ten of 12 of the patients who progressed at CNS were HER2+ve (5) or TNBC (5) and 9 patients had isolated CNS failure. The median overall survival of the 38 patients was 20.4 months (95% CI, 17.4-23.4). Multivariate logistic regression analysis identified non-HR+ve group (OR=2.025, p=0.005) and presence of lymphovascular invasion (OR=5.546, p=0.001) as independent predictive factors of early failure within 12 months following NAC.

Conclusion : Some portion of the patients with LABC may do not have any benefit from NAC, especially for patients with HER2+ and TNBC. In addition to this, our results suggested early CNS failure might be occult CNS metastasis before NAC or curative surgery, which needs to be considered surveillance for occult CNS metastases in high risk patients.

FP03-7

CAN POST OPERATIVE RADIOTHERAPY ADVERSELY AFFECT FLAP BASED IMMEDIATE SKIN SPARING MASTECTOMIES AND RECONSTRUCTIONS?

Eric Drabble*

Breast Unit, Derriford Hospital, United Kingdom

Background/Purpose : Many surgeons and oncologists have traditionally avoided giving radiotherapy to immediate reconstructions for fear of adversely affecting them, and avoided offering immediate reconstruction to patients requiring such adjuvant therapy for fear they were at increased risk of local recurrence.

Methods : Outcomes of 49 patients following skin sparing mastectomy (SSM), immediate flap based reconstruction, and then radiotherapy, over 12 years, were determined by assessing case records and electronic radiology and histology databases. Patients received 45 or 50Gy. All patients underwent analysis of fat biopsies from skin flaps to detect any residual breast tissue. 44 received chemotherapy.

Results : Twenty eight patients underwent TRAM flap reconstruction, 9 with extended latissimus dorsi (LD) flaps, 12 with LD flaps and implants. No patient suffered a local recurrence. Seventeen suffered systemic recurrence. No mastectomy flap biopsy yielded breast tissue. One TRAM flap and one LD flap were lost due to infection. One TRAM flap and 2 LD flaps shrank significantly, 2 TRAM flaps mildly. Overall cosmetic outcomes were judged as good for 29, moderate for 15, poor for 3, unrecorded for 2.

Conclusion : Radiotherapy post SSM and flap based reconstruction is a safe and effective adjunct facilitating immediate reconstruction at mastectomy for larger and higher risk tumours.

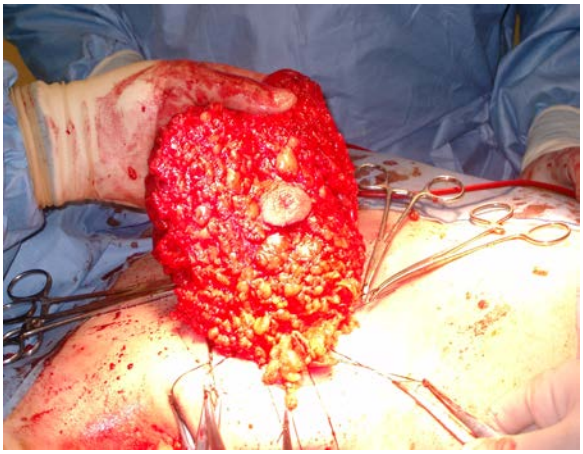

Figure 1

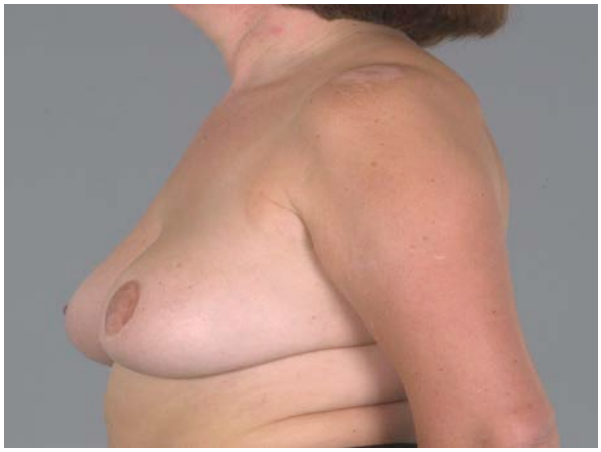

Figure 2

FP03-8

A SINGLE-INSTITUTION COMPARISON BETWEEN APBI (ACCELERATED PARTIAL BREAST IRRADIATION) USING MULTICATHETER BRACHYTHERAPY AND WBI (WHOLE BREAST RADIATION) IN BREAST CANCER WITH "CAUTIONARY" OR "UNSUITABLE" BY ASTRO GUIDELINE

Kazuhiko Sato[1], **Yoshio Mizuno**[2*], **Hiromi Fuchikami**[2*], **Naoko Takeda**[2*], **Masahiro Kato**[3*]

[1] *Breast Oncology Center, Tokyo-West Tokushukai Hospital, Japan*
[2] *Dept. of Breast Oncology, Tokyo-West Tokushukai Hospital, Japan*
[3] *Dept. of Radiation Oncology, Tokyo-West Tokushukai Hospital, Japan*

Background/Purpose : The ASTRO (American Society for Radiation Oncology) issued a consensus statement regarding patient selection for APBI (accelerated partial breast irradiation) following breast-conserving surgery (BCS). However, those categories might not be based on data of ipsilateral breast tumor recurrence (IBTR) risk with APBI. We reviewed our single-institution experience with APBI using multicatheter brachytherapy and whole breast radiation (WBI) in patients considered to be "cautionary" or "unsuitable" by the guideline.

Methods : Of 299 consecutive patients who underwent BCS followed by radiotherapy since November 2007, 183 who received APBI (84 "cautionary" and 99 "unsuitable") and 116 (24 "cautionary" and 82 "unsuitable") who received WBI were analyzed.

Results : Median follow-up was 2.5 years. The IBTR/regional recurrence were observed 2/1 (1.1/0.5%) in the APBI and 4/1 patients (3.4/0.9/%) in the WBI group, respectively.

Conclusion : Although this study was based on a small number of patients with a short follow-up period, the clinical efficacy of APBI for local control after BCS was comparable to that of WBI in patients considered ''cautionary'' or "unsuitable" for APBI by ASTRO guideline.

FP03-9

ONCOLPASTIC BREAST-CONSERVING SURGERY WITH INTERCOSTAL ARTERY PERFORATOR FLAP

Jung Dug Yang[1], Jeong Woo Lee[1], Jin Gu Kang[2], Hyang Hee Choi[2], Seung Ook Hwang[2], Wan Wook Kim[2], Jin Hyang Jung[2], Ho Yong Park[2], Young Ha Lee[3]

[1] *Dept. of Plastic and Reconstructive Surgery, Kyungpook National Univ., Korea*
[2] *Dept. of Surgery, Graduated School of Medicine, Kyungpook National Univ., Korea*
[3] *Dept. of Surgery, Hyosung Hospital, Korea*

Background/Purpose : Oncoplastic breast-conserving surgery (BCS) has been used widely as a treatment protocol for breast cancer. One of them, intercostal artery perforator (ICAP) flap provides adequate coverage without sacrificing any muscle and enables a linear inconspicuous closure of the donor site. Therefore, the oncoplastic volume replacement techniques using local flap which can cover the volume of breast enough were indicated, especially ICAP flap was suggested. This study describes the use of ICAP flap techniques in partial breast reconstruction.

Methods : From March 2011 to August 2012, 31 patients underwent the breast reconstruction with ICAP flap, who had small- to moderate-sized defect on the breasts. Preoperative Doppler ultrasound examination revealed the good intercostal artery perforators, and the ICAP flap was outlined. ICAP flap can be classified according to the pedicle. Lateral ICAP flap is based on the perforators arising from the costal segment on the lateral aspect of the thorax (Fig. 1) and inframammary ICAP flap is based on the perforators from the muscular segment (Fig. 2). Regarding the lateral region, the perforators are usually located between 3 and 4.5 cm from the anterior border of the latissimus dorsi (LD) muscle (sixth and seventh intercostal spaces). Regarding the medial region, the perforators are usually located within 1-4 cm lateral to the sternal border. The incision was carried down to the serratus anterior and LD muscles in the lateral ICAP flap or to the pectoralis muscle or the rectus abdominis muscle in the inframammary ICAP flap. The elevated flap was inset to the defect through the tunnel and the inframammary fold was reinforced with non-absorbable suture. The donor site was closed primarily.

Results : The mean age was 46.7 years, and the average follow-up interval was 6 months. Patients were divided into 4 groups according to the location of tumor (upper outer quadrant (UOQ) groups, 10; lower outer quadrant (LOQ) group, 15; lower inner quadrant (LIQ) groups, 4; central groups, 2). The average specimen weight was 109.2 g. Complications developed in 4 cases, including 3 cases of venous congestion, but self-limited, and 1 case of wound dehiscence on the donor site of inframammary fold. The majority of patients were satisfied with their cosmetic outcomes.

Conclusion : ICAP flap technique can be reliable and useful technique in correcting breast deformity after BCS, especially in the patients who had small- to moderate-sized defect on the breasts.

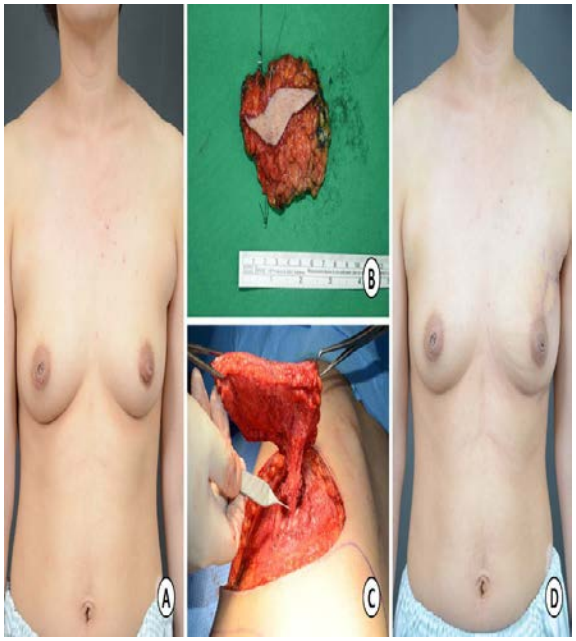

Figure 1

A 45 year-old woman with invasive ductal carcinoma (IDC) in the left breast. (A) Preoperative view. (B) The excised volume of partial mastectomy was 60g. (C) Intraoperative view of the elevated lateral intercostal artery perforator (ICAP) flap. The tip of Adson forceps indicates the intercostal artery perforator. (D) 1-month postoperative outcome.

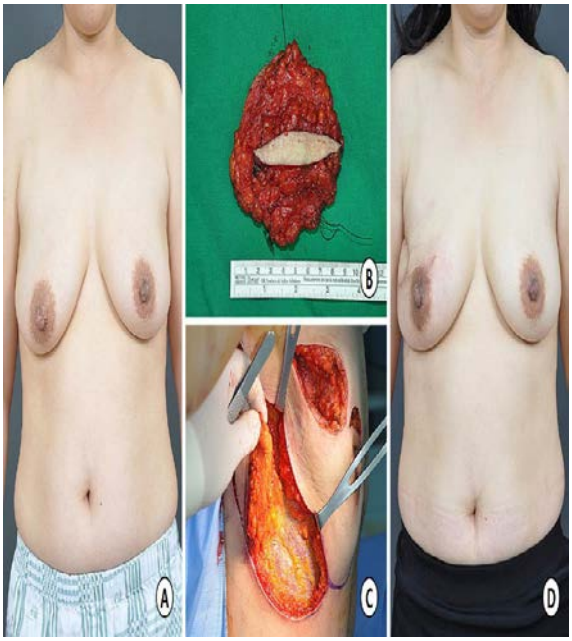

Figure 3

A 50 year-old woman with IDC in the right breast. (A) Preoperative view. (B) The excised volume of partial mastectomy was 95g. (C) Intraoperative view of the elevated inframammary ICAP flap. (D) 4-month postoperative outcome.

FP04-1

THE EFFECTS OF BREAST HEALTH EDUCATION PROGRAM BASED ON SELF-EFFICACY THEORY AND PERSONAL NARRATIVE ON SELF-EFFICACY, KNOWLEDGE, AND RESILIENCE IN WOMEN WITH BREAST CANCER

Myungsun Yi, Young Mi Ryu*, Jieun Cha

College of Nursing, Seoul National Univ., Korea

Background/Purpose : Breast cancer is one of the major cancers among women in Korea. Although the survival rates of breast cancer are relatively higher than the other cancers, women with breast cancer still suffer from all aspects of life. Therefore, it is important for them to overcome these obstacles. Self-efficacy theory is known to be effective in improving ability to influence events that affect their lives. Personal narrative is also considered to be powerful as a therapeutic tool not only for themselves but also for others. The purpose of the study was to investigate the effects of breast health education program based on self-efficacy theory and personal narrative on self-efficacy, knowledge, and resilience in women with breast cancer in Korea.

Methods : The study used a nonequivalent control group posttest only design. The 3-day program designed to educate breast cancer survivors to become lecturers of breast cancer prevention was implemented. The program consisted of sharing breast cancer experiences as well as the lectures on breast cancer and breast self-examination. Thirteen breast cancer survivors participated in the experimental group and 23 in the control group. The data were collected using questionnaires in 2013.

Results : The experimental group and control group were equivalent based on demographic and illness related characteristics. The levels of self efficacy, knowledge, and resilience were significantly higher in the experimental group compared to the control group ($p<0.05$).

Conclusion : The results of the study indicate that women with breast cancer could be resilient to overcome various impediments they face as a breast cancer survivors by receiving breast health education based on self-efficacy theory and personal narrative. Further studies are need to identify long term effects of the program.

FP04-2

QUALITATIVE ANALYSIS OF WOMEN'S KNOWLEDGE, ATTITUDES AND EXPERIENCES REGARDING URINARY SYMPTOMS ASSOCIATED WITH AROMATASE INHIBITORS FOR EARLY STAGE BREAST CANCER

Mariana De Souza E Sousa[1*], **Bettina Meiser**[1], **Michael Friedlander**[2], **Martha Hickey**[3], **Sherin Jarvis**[4], **Michelle Peate**[1], **Craig Lewis**[2]

[1] *Prince of Wales Clinical School, Univ. of New South Wales, Australia*
[2] *Dept. of Medical Oncology, Prince of Wales Hospital, Australia*
[3] *Dept. of Obstetrics and Gynaecology, The Royal Women's Hospital, Australia*
[4] *Dept. of Endo-Gynaecology, The Royal Hospital for Women, Australia*

Background/Purpose : With ongoing advances in early detection and treatment effectiveness, women are living longer with breast cancer. With such promising outcomes many women are advised to consider the long-term effects of a cancer diagnosis including the side effects of treatment on long-term quality of life. Urinary symptom as a result of adjuvant endocrine therapy is one concern. Research in this area is lacking, especially in specific group populations such as women on endocrine treatment modalities, whose views are not well described to date. This study aimed to explore views and experiences of living with urinary symptoms and associated quality of life and sexual issues among postmenopausal women receiving aromatase inhibitors. In addition, it sought to increase understanding of health-care-seeking behavior, treatment expectations and degree of satisfaction regarding the current provision of information.

Methods : We developed a semi-structured interview guide to elicit the knowledge, attitudes and experiences of postmenopausal women receiving aromatase inhibitors for early breast cancer regarding urinary concerns and related quality of life and sexual issues. Interviews were conducted until thematic saturation was reached. Multiple thematic analysis of data was undertaken following verbatim transcription.

Results : We conducted 11 in-depth interviews with postmenopausal women on aromatase inhibitors recruited from a major teaching hospital in NSW. Urinary symptoms were described as impacting adversely on several activities in daily life, for instance, in simple tasks such as driving around. Among women with a partner, urinary disorders did not impact as severely on sex life as breast cancer diagnosis and treatment. Help-seeking behavior was hindered mostly because of the feeling that urinary concerns were not a major health problem in their lives compared with breast cancer. Additional barriers were lack of knowledge, perception that symptoms were not sufficiently severe and costs of treatment. Most participants thought that a meaningful treatment outcome would be to prevent the onset of new symptoms. The majority of women reported a lack of available information and indicated preference for paper-based methods of communication such as pamphlets and also information provided by either their general practitioner or oncologist.

Conclusion：We recommend development of interventions that aid early identification and acknowledgment of symptoms in order to facilitate help seeking as well as improving awareness of health professionals to informing women about available treatment options.

FP04-3

FACTORS INFLUENCING QUALITY OF LIFE IN BREAST CANCER PATIENTS WITH HORMONE THERAPY

Eunkyung Hwang[1*], **Myungsun Yi**[2]

[1] *Breast Care Center, Seoul National Univ. Hospital, Korea*
[2] *College of Nursing, Seoul National Univ., Korea*

Background/Purpose : In Republic of Korea, approximately 13,000 women are diagnosed with breast cancer annually. And the improvements in diagnosis and treatment have led to longer survival of these patients. Hormone therapy is one of the major treatments, contributing to survival rates of breast cancer patients. At the same time, however, numerous side effects and complications due to hormone therapy have been reported in the literature. The purpose of the study was to identify degrees of pain, menopause symptoms, and quality of life, and to identify correlations between these variables, and finally to identify factors influencing quality of life of breast cancer patients with hormone therapy.

Methods : A cross-sectional survey design was utilized. The data were collected from 110 breast cancer patients with hormone therapy for more than 3 months from a university hospital in Seoul. The quality of life was measured by Functional Assessment of Cancer Therapy-Breast , pain by Korean Version of Brief Pain Inventory and Menopause symptom by Menopause Rating Scale. The data were analyzed using χ^2 test, t-test, ANOVA, pearson correlation coefficient and multiple linear regression.

Results : Most of the participants (88.2%) reported to have pain, The average score of pain was 28.83, with 17.78 of pain interference and 10.27 of pain severity. The most painful area was the operation area. Patients with aromatase inhibitor had more muscular-skeletal pain, when compared to those with other hormone therapy. Compliance with hormone therapy was significantly different by increased pain ($p=0.001$). Most of the participants (95.5%) reported having menopause symptoms. The average score was 18.32, and 60.0% of them indicated that they have a severe degree of menopause symptoms. The average score of quality of life was 87.84±21.17. Pain, menopause symptom and quality of life had strong correlation with each other ($p<0.005$). Quality of life was explained by menopause symptom ($\beta=-0.705$), economic status ($\beta=0.202$) and occupation ($\beta=0.155$).

Conclusion : In conclusion, most breast cancer patients with hormone therapy suffer from pain and menopause symptoms. And the quality of life of them were influenced mainly by menopause symptoms. Therefore, intervention, including menopause symptoms reduction guidelines should be incorporated in oncologic nursing care to alleviate menopause symptoms and pain, and finally to improve quality of life of breast cancer patient with hormone therapy.

FP04-4

FEAR OF RECURRENCE AFTER BREAST CANCER TREATMENT

Soo Jung Park[1], **Im-Ryung Kim**[2], **Danbee Kang**[1], **Juhee Cho**[2]

[1] *Dept. of Health Science and Technology, Samsung Advanced Institute for Health Sciences & Technology, Sungkyunkwan Univ., Korea*
[2] *Cancer Education Center, Samsung Comprehensive Cancer Center, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : Breast cancer patients often feel lost when they complete a primary treatment. Being departed from their regular treatment life, they are facing a challenge to manage their health and fear or recurrence. Despite a possible impact of fear of recurrence on patients' quality of life, little study has been done. Especially, scanxiety, the word from combination of scan and anxiety, is the field that yields so much to discover.

Methods : We purposely recruited 30 breast cancer patients at a tertiary hospital in Seoul, Korea, whose time since completion of cancer treatment has been at least a year. Semi-structured interview was performed on each participant for an hour, and participants were asked to complete questionnaires for socio-demographics and clinical information. All interviews were recorded and transcribed into text. Collected data were thematically analyzed specifically focusing on fear of recurrence and scanxiety.

Results : Most participants said they keep having fear of recurrence especially when they have regular follow-up examination. About half of them (13 patients, 43.3%) said that they experienced psychological anxiety disorder because of this fear of recurrence. Participants told they experienced fear of recurrence when they have physical pain or symptoms such as muscle ache and pain on breast. Six participants said they got easily agitated when exposed to any depressing words including obituary. They also expressed they had a lot of distress to keep healthy lifestyles and those stressors sometimes made them have psychological problems such as insomnia or depression. Moreover, one third (9 patients, 30%) of participants suffered from scanxiety, which is the anxiety cancer patients undergo particularly before and after scan or regular follow-up, in addition to fear of recurrence. While they have substantial needs of information regarding life management after cancer, survivors were not able to find appropriate materials of education. Especially, participants look for information for managing fear of recurrence.

Conclusion : While some participants say they feel very relieved after tightly scheduled treatments, many others are extremely stressed out from being apart from their physicians. They frequently experienced fear of recurrence, some with scanxiety as well, and had difficulties to manage life after cancer. Health professionals should pay more attention to evaluate breast cancer patients' psycho-social needs after completion of treatment and provide appropriate informational support.

FP04-5

ASSOCIATED FACTORS WITH CHANGES IN COGNITIVE FUNCTION IN BREAST CANCER PATIENTS RECEIVED CHEMOTHERAPY (BASED ON THE CONCEPTUAL MODEL OF CHEMOTHERAPY-RELATED CHANGES IN COGNITIVE FUNCTION)

Kayoung Shin[1], **Jeehee Han**[2*], **Sue Kim**[2], **Yunhee Ko**[1], **Keonsul Lee**[3], **Kyunghee Lim**[4], **Hyejin Joh**[5], **Eunkyung Hwang**[6], **Kyunghi Lee**[7], **Dongmi Kim**[3]

[1] *College of Nursing, Yonsei Univ., Korea*
[2] *Dept. of Family Health Science, College of Nursing, Yonsei Univ., Korea*
[3] *Center for Breast Cancer, National Cancer Center, Korea*
[4] *College of Nursing, Keimyung Univ., Korea*
[5] *Dept. of General Surgery, The Catholic Univ. of Korea Seoul St. Mary's Hospital, Korea*
[6] *Breast Care Center, Seoul National Univ. Hospital, Korea*
[7] *Dept. of Nursing, Yonsei Univ. Severance Hospital, Korea*

Background/Purpose : An increasing body of literature presents influence factors of cognitive function in breast cancer patients receiving chemotherapy. However few studies have approached on the theoretical basis. From this aspect, this study aims to confirm associated factors (physiologic factors, psychosocial factors, situational factors, concurrent symptoms) based on the conceptual model of chemotherapy-related changes in cognitive function.

Methods : (Preliminary report: The data will be collected by August and further analysis is planned) The data have been collected using structured self-reporting questionnaires including scales of cognitive impairment, fatigue, depression, pain and social support for 250 patients in ward and outpatient clinic of 5 general hospitals. Statistical Package, SAS 9.2 was used for statistical analysis of t-test, ANOVA, correlation analysis, regression and AMOS 21.0 for covariance structural analysis.

Results : (Preliminary report) Breast cancer patients received chemotherapy appeared to show a high level of cognitive impairment, depression and fatigue. Among physiologic factors, the effect of frequency of chemotherapy was found to be statistically significant on cognitive impairment. Intensity of depression on psychosocial factors was negatively associated with cognitive function and control of life style as moderate exercise and social support on situational factors had positive affect to cognitive function. Concurrent symptoms as fatigue and pain had significant correlation with physiologic factors. By structural modeling, the domain of situational factors had higher level of explanation then other domains.

Conclusion : These findings support the usefulness of conceptual model of chemotherapy-related changes in cognitive function and help understanding cognitive impairment in breast cancer patients received chemotherapy. Furthermore it can be used to develop appropriate, effective nursing interventions using the conceptual model of chemotherapy-related changes in cognitive function.

FP04-6

DEVELOPMENT AND VALIDATION OF CHEMOTHERAPY-INDUCED ALOPECIA DISTRESS SCALE (CADS) FOR BREAST CANCER PATIENTS

Juhee Cho[1], Eun-Kyung Choi[1], Hee-Soon Juon[2], Im-Ryung Kim[1], Young-Hyuck Im[3], Yeon Hee Park[3], Soohyun Lee[4], Jeong Eon Lee[5], Jung-Hyun Yang[6], Seok-Jin Nam[5*]

[1] *Cancer Education Center, Samsung Medical Center, Korea*
[2] *Dept. of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, U.S.A.*
[3] *Dept. of Medical Oncology, Samsung Medical Center, Korea*
[4] *Dept. of Medical Oncology, Yonsei Univ., Severance Hospital, Korea*
[5] *Dept. of Surgery, Samsung Medical Center, Korea*
[6] *Dept. of Surgery, Konkuk Univ. Medical Center, Korea*

Background/Purpose : This study developed and validated the Chemotherapy-induced Alopecia Distress Scale (CADS) that evaluate psychosocial distress that women with breast cancer experience because of the hair loss during chemotherapy.

Methods : Twenty-five items for chemotherapy-induced alopecia distress was developed based on a qualitative study, and a cross-sectional survey was conducted with 305 Korean women with breast cancer. To extract factor structure and evaluate construct validity, exploratory and confirmatory factor analysis was performed. Concurrent and discriminant validity were tested by correlations with the psychosocial factors. In addition, external validity analysis was conducted using data from another prospective study of 428 breast cancer patients.

Results : Exploratory factor analysis and confirmatory factor analysis yielded 17 items in four domains and the model fit was good (CFI=0.925). Coefficient alphas ranged from 0.77 to 0.95 for subdomains and 0.95 for total and it was similar with the validation dataset confirming its external validity. Total CADS scale was moderately correlated with body image (r=-0.47, P<0.001), more weakly correlated with the patients' overall QOL (r=-0.28, P<0.001), but did not correlate with self-esteem (r=-0.07, P=0.23).

Conclusion : Our study confirmed that the CADS consists of 17 items in four domains (physical, emotional, activity, and relationship) and it reports good reliability and validity tool for measuring distress of chemotherapy-induced alopecia in women with breast cancer.

Figure 1 Path diagram 17 item of Chmotherapy-induced Alopecia Distress CFA model (N=305)

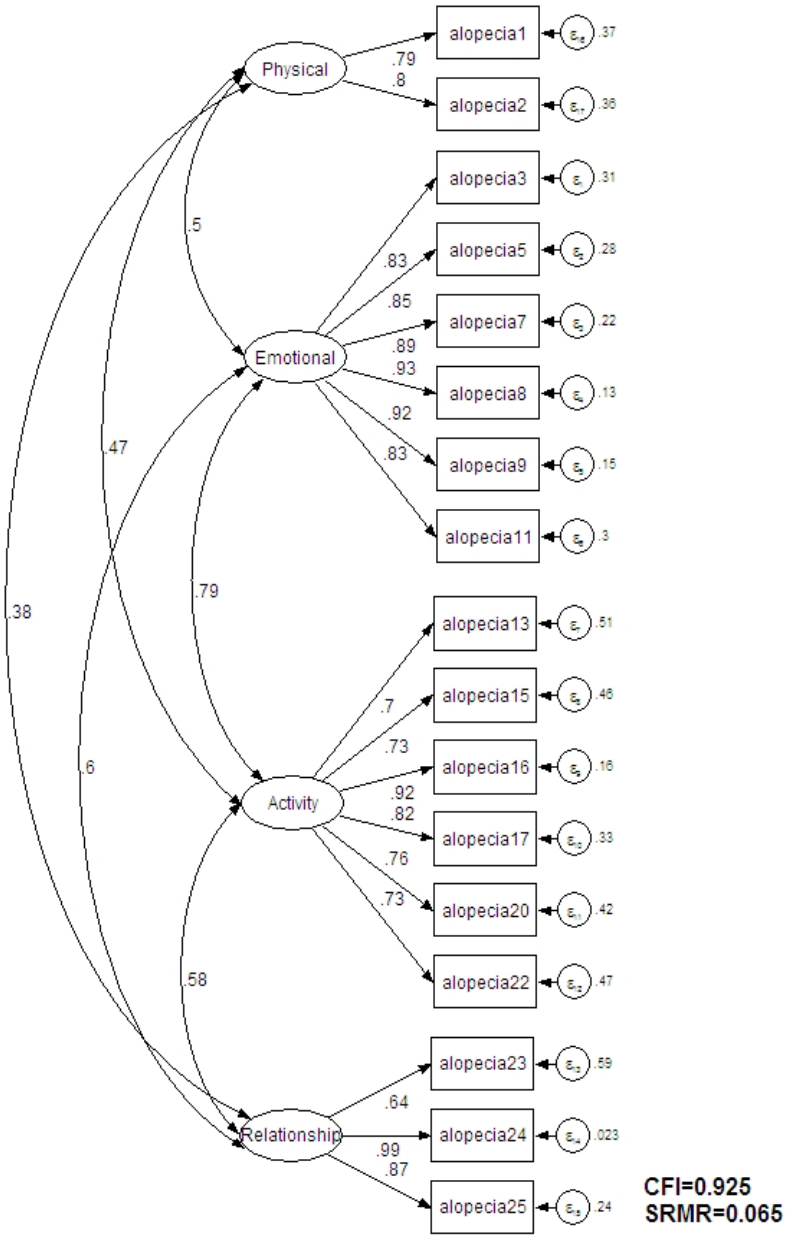

Figure 1

FP04-7

EXPERIENCE OF IRANIAN MEN IN LIVING WITH A SPOUSE WITH BREAST CANCER

Fariba Taleghani[1*], **Ahmad Nasiri**[2], **Alireza Irajpour**[3]

[1] *Nursing & Midwifery Care Research Center, Isfahan Univ. of Medical Sciences, Iran*
[2] *Faculty of Nursing & Midwifery, Birjand Univ. of Medical Sciences, Iran*
[3] *Faculty of Nursing & Midwifery, Isfahan Univ. of Medical Sciences, Iran*

Background/Purpose : Breast cancer is the most common cancer among women. In Iran, breast cancer is in the first rank in malignant cancers among Iranian women and has the highest prevalence. Although cancer is a stressful event for all family members, one of the most important social and familial consequences of breast cancer is its effect on the spouses of these patients. Spouses' trust and support are crucial for a patient in stages of diagnosis and treatment of cancer. As patients' spouses often accept the role of a caregiver with the lowest preparation and support, if their concerns, remain unknown, the problems will not be solved, so exploration of men's adaption process to their spouses' cancer can be helpful in provision of care and manner of their dealing with their spouses' disease

Methods : This is a qualitative study conducted based on grounded theory. Participant comprised the men whose spouses had breast cancer and selected from various social and economic classes and interviewed. Sampling continued until data saturation and ended with total of 26 participants. Constant comparative method was used to analyze the data in this study.

Results : Results of the present study showed that men's adaptation with their spouses' breast cancer is a process which starts from the moment of disease diagnosis and occurs in three stages of exposure to crisis, insertion of life-course disruption and struggle to modify disruption in life. The first stage of men's exposure to their spouses' disease is the exposure to crisis. The happenings in this stage indicate the fact that cancer leaves the spouse in a sudden shock and is accompanied with unpleasant psychological and mental reactions. Family disruption, heavy shadow of disease on marital relationship, concerns associated to disease management, and resistance against disruption in life are the main categories which formed the second stage of men's exposure to their spouses' disease. Revising the relationship with the relatives',' emotional and functional support to the spouse', “trying to improve marital relationship” and 'seeking support to modify disruption in life' formed the third stage of men's exposure to their wives' breast cancer as ' struggle to modify disruption in life'. Men gradually found out that they could not live in the way before their spouses' disease and had to revise many aspects of their life. Therefore, a struggle to modify disruption in life was administered and they constantly tried to compensate the defects.

Conclusion : Results declared the necessity for these men's support and conduct toward use of efficient coping strategies. Nurses can plan to facilitate the men’s adaptation to the conditions by supporting and helping them through an accurate primary and comprehensive assessment of their psychological status, experiences and investigation of their used strategies. Nurses should support men's struggle to modify the disruption in life and facilitate their adaption to the disease of their spouses through appropriate interventions.

FP04-8

A VALIDATION STUDY OF CANCER STIGMA SCALE FOR KOREAN PATIENTS (CSS-K)

Hyang Sook So[1], **Ae Ran Park**[2], **Myeong Jeong Chae**[3]

[1] *College of Nursing, Chonnam National Univ., Korea*
[2] *Dept. of Nursing in Graduate School, Chonnam National Univ., Korea*
[3] *Dept. of Nursing, Gwangju Woman's Univ., Korea*

Background/Purpose : To identify validity of the Cataldo Lung Cancer Stigma Scale (CLCSS, Cataldo, 2011) to be fit for Korean patients with cancer. There are no stigma scale for cancer patient in Korea yet.

Methods : Cancer Stigma Scale for Korean Patients (CSS-K) was validated as follows; modification of item questions and content validity, pilot study, and psychometric tests. A total of 260 patients diagnosed with stomach, lung, colon, breast, or cervix cancer undergoing anti-cancer therapy were recruited from outpatient clinics and inpatient oncology units of a regional national cancer center under permit from Institutional Review Board (No: 2012-167). The patients were asked to complete self-reported questionnaire comprising the revised content-validated thirty items, and also the Distress scale (National Comprehensive Cancer Network, 2003) and SGSS (Social Guilt and Shame Scale, Sanftner & Tangney, 1994) for criterion-related validity. A confirmatory factor analysis of stigma scale was used for construct validity. The obtained data were analyzed using descriptive statistics, factor analysis, simple correlation, and Cronbach's alpha.

Results : Preliminary thirty one items which had generated for lung cancer through translation and reverse translation process (Lee & Kim, 2011) was transformed in order for measuring Korean cancer patients by revision and content validity. Six factors were extracted by factor analysis & varimax rotation: social isolation (5 items), discrimination (4 items), distancing or a voiding (4 items), guilty (5 items), attribution (3 items), and refuse feeling from medical staff(4 items). A total of 25 items was loaded on one factor with ranges of 0.47-0.85. Only eight items were loaded on two factors with over 0.35. The amount of total variance explained by six factors was 62.4% (Table 1). Cronbach's alpha coefficient was 0.89. The final version of Cancer Stigma Scale Korea version (CSS-K) was consisted of twenty five items. The correlation between scores of stigma (CSS-K) and shame/ guilt (SGSS) were strongly associated, and then means that CSS-K was tested the criterion-related validity ($r=0.589$, $p<.001$). Discrimination and guilty of stigma subscales were associated with guilt subscale of SGSS strongly ($r=0.501$ and $r=0.504$, $p<0.001$), and also guilty and attribution of stigma subscales were with shame moderately ($r=0.438$ and $R=0.449$, respectively). Also stigma was associated with symptom distress and life disturbances slightly ($r=0.320$ and $r=0.356$, respectively) (Table 2). The CSS-K was established construct validity, criterion-related validity, and reliability with stability.

Conclusion : The newly validated CSS-K with 25 items is an clinically applicable measure for general cancer patients. It is recommended for further study to identify the predictive and discriminant validity among cancer patients in order to establish the strong measure. This study is contributed to stimulate clinical psycho-oncology research and practice.

Table 1. Factor loadings of stigma scale (CSS-K) items with varimax rotation

	Statement	Factor					
		I. Social Isolation	II. Distancing / Avoiding	III. Discrimination	IV. Guilty	V. Attribution	VI. Refusing Tx. of Med staff
11	I have lost friends by telling them I have a cancer	.809	.154	-.029	.207	.045	.128
13	People have physically backed away from me	.725	.175	.319	.220	.072	.046
15	People seem afraid of me because I have a cancer	.721	.336	.232	.049	.088	.144
14	People I care about stopped calling after learning that I have a cancer	.673	.454	.172	.118	.216	-.010
12	I stopped socializing with some because of their reactions	.603	.039	.517	.038	-.034	-.025
17	I stopped socializing with some because of their reactions	.205	.775	.053	.061	.085	.194
16	People avoid touching me if they know I have a cancer	.171	.709	.064	.085	.168	.022
18	People avoid you because a cancer is associated with death.	.150	.675	.387	.221	-.038	.003
19	Some people who know have grown more distant	.267	.619	.433	.168	-.044	.006
22	People with a cancer are treated like outcasts	.192	.247	.743	.068	.150	-.029
21	I worry about people discrimi--nating against me	.147	.164	.702	.121	.320	.105
25	I worry that people may judge me when they learn I have a cancer	.073	.090	.502	.255	.403	.192
20	I was hurt how people reacted to learning I have a cancer.	.293	.403	.495	.083	.175	.130
3	Having a cancer makes me feel like I'm a bad person.	.111	.154	.091	.762	-.017	.096
5	Having a cancer makes me feel unclean.	.093	-.037	.016	.747	.136	-.038
4	I feel I'm not as good as others because I have a cancer	.014	.091	.258	.718	.089	.249
1	I feel guilty because I have a cancer.	.220	.241	-.039	.649	.250	.080
6	I feel set apart, isolated from the rest of the world.	.320	.175	.361	.504	-.144	.271
27	Cancer is viewed as a self- inflicted disease.	.014	.149	-.071	.080	.742	.047
29	Others assume that a patient's cancer was caused by poor life habits, even if he or she never had	.074	.126	.285	.058	.717	.123
28	Some people act as though it is my fault that I have a cancer.	.049	-.049	.208	.046	.647	.012
9	My cancer diagnosis was delayed because my healthcare provider did not take my alarm sign seriously.	.030	.071	.076	.073	-.023	.852
30	Healthcare provider don't take early signs of cancer seriously (ex: coughing, bowel habit change, lumps, abnormal bleeding)	-.082	-.014	.219	.157	.282	.591
10	People who have high-risk factor (smoking, obese, salty diet intake, genetic)could be refused treatment for the cancer	.316	.147	-.159	.080	.056	.521
8	Some told me a cancer is what I deserved for poor health habits	.209	.049	.073	.177	.484	.466
Eigen value		3.16	2.77	2.76	2.70	2.33	1.88
Total Variance Explained	62.37	12.65	11.07	11.04	10.78	9.32	7.51
Cronbach's alpha coefficients	.890	.864	.800	.799	.787	.644	.615

*CSS-K : cancer stigma scale - Korea version

Table 1

<Table 2> Relationships between stigma (CSS-K), self-blame, and distress

(N = 247)

Measure	Total Score	Subscale of Stigma					
		I. Social Isolation	II. Distancing / Avoiding	III. Discrimination	IV. Guilty	V. Attribution	VI. Refusing Tx. of Med staff
		r (p)					
SGSS total	.589***	.340***	.258***	.497***	.523***	.423***	.394***
Subscale 1 Guilt	.561***	.386***	.292***	.501***	.504***	.306***	.315***
Subscale 2 Shame	.500***	.231***	.175*	.396***	.438***	.449***	.391***
Distress B							
Symptom	.320***	.234***	.094	.370***	.282***	.128*	.191**
Life disturbance	.356***	.252***	.132*	.321***	.329***	.097	.300***

*** <.001 ** <.01 * <.05

Table 2

FP05-1

PROGNOSTIC RELEVANCE OF BIOLOGICAL SUBTYPE OVERRIDING TNM STAGING IN BREAST CANCER: DISCORDANCE BETWEEN STAGE AND BIOLOGY

Hyun Ae Jung[1], Yeon Hee Park[1], Moon Ki Choi[1], Jung Yong Hong[1], Seok Won Kim[2], Won Ho Kil[1], Jeong Eon Lee[2], Seok Jin Nam[2], Jin Seok Ahn[1], Young-Hyuck Im[1*]

[1] *Division of Hematology-Oncology, Dept. of Medicine, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

[2] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : Recently, we face “on the edges” for treatment decision to decide adjuvant systemic treatment, especially for patients who show discordance between stage and biology. There is an area which needs to be special consideration because of their aggressive tumor biology irrespective of TNM stage. On the contrary to this, there is some portion of the patients who do not have any benefit from adjuvant chemotherapy in spite of advanced stage. The aim of this study was to compare prognostic relevance of TNM staging system with intrinsic subtype in breast cancer who received curative surgery.

Methods : We retrospectively identified patients who received curative surgery for stage I-III breast cancer and had immunohistochemistry profile including hormone receptor status, human epidermal growth factor receptor 2 (HER2) and Ki 67 staining at Samsung Medical Center from January 2004 to September 2008. Primary outcomes were recurrence free survival (RFS) and overall survival (OS).

Results : One thousand one hundred and forty five patients were diagnosed of breast cancer and received curative surgery. Four hundred-sixty three (40.4%) patients was stage I and 682 (59.6%) patients was stage II and III. Among them, 847 (74.0%) patients was hormone receptor (HR)-positive, 239 (20.9%) was HER2 positive and 205 (20.9%) patients was triple negative breast cancer. 5-year RFS of the patients who had HR-positive and HER2-negative with and Ki-67 staining 1+ (0-25%) was 99%. 5-year RFS for HER2 positive and triple negative breast cancer patients was 84% and 82% ($p<0.001$, respectively) In multivariate analysis, advanced stage (II/III) and aggressive biology (HER2 positive or triple negative) retained their statistical significance to predict poorer RFS and OS. The patients with advance stage disease (II or III) but favorable tumor biology (HR positive and HER2 negative and Ki-67 1+) had better clinical outcomes than those of stage I with unfavorable tumor biology (HER2 positive or triple negative) in terms of RFS (5-year RFS rate 99% vs. 89%, $p=0.02$) and OS (5-year OS rate 99% versus 93%, $p=0.03$).

Conclusion : The current results showed that intrinsic subtype had overriding prognostic impact in subpopulation of stage I-III breast cancer. Discordance between stage and biology may have more critical clinical relevance for establishing therapeutic strategy to predict clinical outcomes than stage.

Figure 1. RFS and OS curves

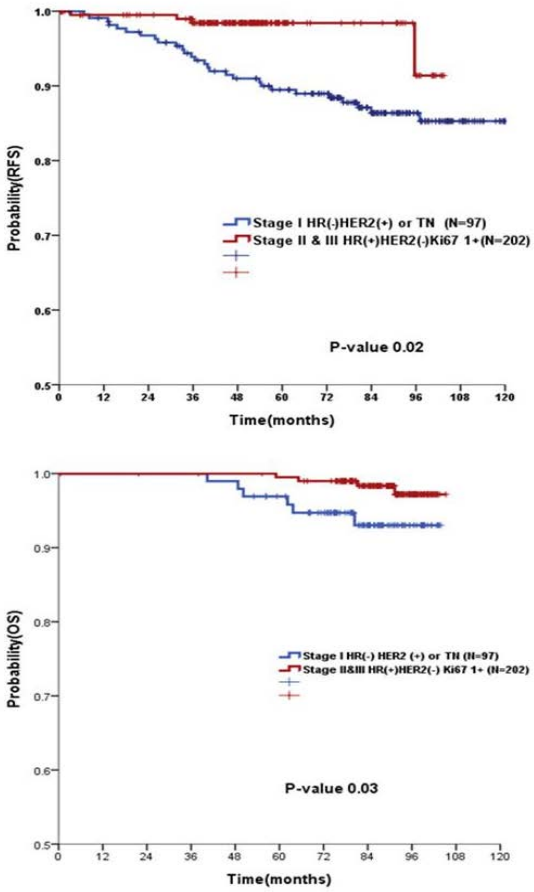

Figure 1

Table 1. Multivariate cox proportional hazard ratio analysis for RFS and OS

		Recurrence free survival			Overall survival		
		HR	95% CI	P-value	HR	95% CI	P-value
Biology	ER(-) HER2 (+) or TN	8.71	3.17-23.88	<0.001	7.39	2.56-21.35	<0.001
Stage	II or III	2.69	1.82-3.97	<0.001	3.21	2.00-5.15	<0.001

Table 1

FP05-2

THE CLINICAL IMPACT OF 21-GENE RECURRENCE SCORE ON TREATMENT DECISION FOR PATIENTS WITH HORMONE RECEPTOR-POSITIVE EARLY BREAST CANCER IN KOREA

Moo Hyun Lee[1], Wonshik Han[2], Jeong Eon Lee[3], Ku Sang Kim[4], Heeseung Park[5], Jongjin Kim[2], Soo Youn Bae[3], Hyunjoo Shin[4], Jong Won Lee[5*], Eun Sook Lee[1*]

[1] *Center for Breast Cancer, National Cancer Center, Korea*
[2] *Dept. of Surgery, College of Medicine, Seoul National Univ., Korea*
[3] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*
[4] *Dept. of Surgery, School of Medicine, Ajou Univ., Korea*
[5] *Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*

Background/Purpose : The 21-gene assay (Oncotype DX) recurrence score (RS) is useful in predicting adjuvant chemotherapy benefit in early breast cancer patients. We analyzed the results from five institutions' experience of using Oncotype DX and examined the impact of the recurrence score on decision making of chemotherapy in Korean breast cancer patients and the associations between RS and prognostic factors.

Methods : Oncotype DX testing was performed in 211 patients with estrogen receptor-positive early breast cancer in five institutions. Each surgeon made systemic treatment decisions both before and after knowledge of the RS.

Results : Among 211 patients, 129 (61.1%) patients had a low RS of <18, 61 (28.9%) an intermediate RS of 18-30, and 21 (10%) a high RS of ≥ 31. Histologic grade, presence of micrometastases, Ki-67 and presence of lymphatic invasion were statistically associated with the RS. Treatment decisions were changed in 113 of 211 patients (53.6%): in 107 of 211 (50.7%) from chemotherapy plus hormone therapy to hormone therapy and in 6 of 211 (2.8%) from hormone therapy to chemotherapy plus hormone therapy.

Conclusion : The 21-gene recurrence score has a significant impact on treatment decision-making. The test reduces chemotherapy use in more than half of Korean estrogen receptor-positive, early breast cancer patients.

FP05-3

IDENTIFICATION OF THE PATIENTS WITH A POOR PROGNOSIS AMONG ESTROGEN RECEPTOR-POSITIVE BREAST CANCER WITH THE INTERMEDIATE ONCOTYPE DX RECURRENCE SCORE

Sung Gwe Ahn[1], **Hak Min Lee**[1], **Hak Woo Lee**[1], **Seung Ah Lee**[1], **Se-Ra Lee**[2], **Sun-Hee Leem**[2], **Joon Jeong**[1*], **In-Sun Chu**[3]

[1] *Dept. of Surgery, College of Medicine, Yonsei Univ., Gangnam Severance Hospital, Korea*
[2] *Dept. of Biology, College of Natural Science, Dong-A Univ., Korea*
[3] *Korean Bioinformation Center, Korea Research Institute of Bioscience and Biotechnology, Korea*

Background/Purpose : The Oncotype DX recurrence score (RS) predictor has been clinically utilized to determine adjuvant chemotherapy among early breast cancer with estrogen receptor (ER) positivity. Adjuvant chemotherapy can be indicated for patients with high RS and spared for patients with low RS. However, decision making of chemotherapy for patients with intermediate RS remains controversial. We tried to discriminate a poor prognosis among ER-positive breast cancer with an intermediate RS based on gene expression profiling (GEP).

Methods : GEP was performed using gene expression data from 297 Korean patients with breast cancer. Five hundred nanograms of total RNA were used for labeling and hybridization, according to the manufacturer's protocols (Illumina, San Diego, USA). RS and the 70-gene-scores (70GS) were calculated based on GEP. Various statistical methods were applied to identify gene signatures correlated with poor 70GS in intermediate RS.

Results : In a total of 297 patients, 82 patients with ER-positivity and the intermediate RS were identified. These patients were stratified by 70GS (Good, 66; Poor, 16) and overall survival (OS) significantly differed according to 70GS (p=0.014). Gene network analysis using Ingenuity Pathway Analysis (IPA) software revealed considerable enrichment of the gene network toward FOXM1 in poor 70GS cluster, suggesting that its activation might be a key determinant associated with a poor prognosis of the patients with the intermediate RS. Also, the expression of several representative genes for cell proliferation, such as AURKA, AURKB, BIRC5, BUB1, CCNDB1, and TOP2A, was significantly higher in poor 70GS cluster than in good 70GS cluster. In the patients with ER-positivity and the intermediate RS, FOXM1, AURKA, AURKB, BIRC5 showed a clinical significance for overall survival (p=0.024, p=0.028, p=0.032, p=0.092, respectively). For overall survival, Harrel's c-indexes were 0.796 with FOXM1, 0.792 with AURKA, 0.755 with AURKB, and 0.821 with BIRC5, respectively. These proliferative gene markers showed 72 to 85% agreement in poor 70GS (FOXM1, 85%; AURKA, 80%; AURKB, 75%; BIRC5, 72%).

Conclusion : 70GS and expression of proliferative genes, such as FOXM1, AURKA, AURKB, and BIRC5, can contribute to discriminate a survival difference in ER-positive patients with the intermediate RS.

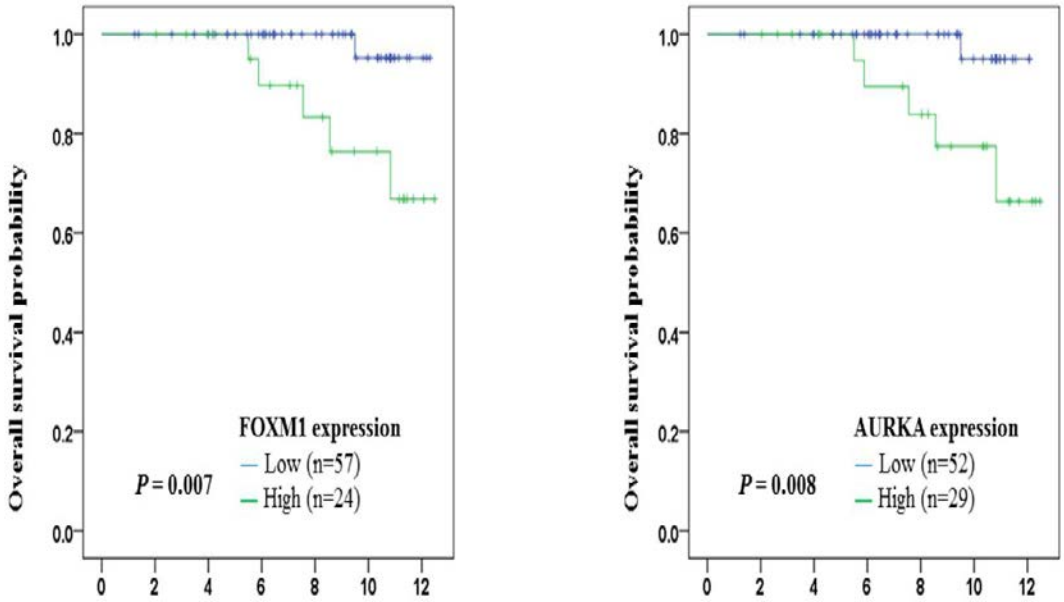

Figure 1

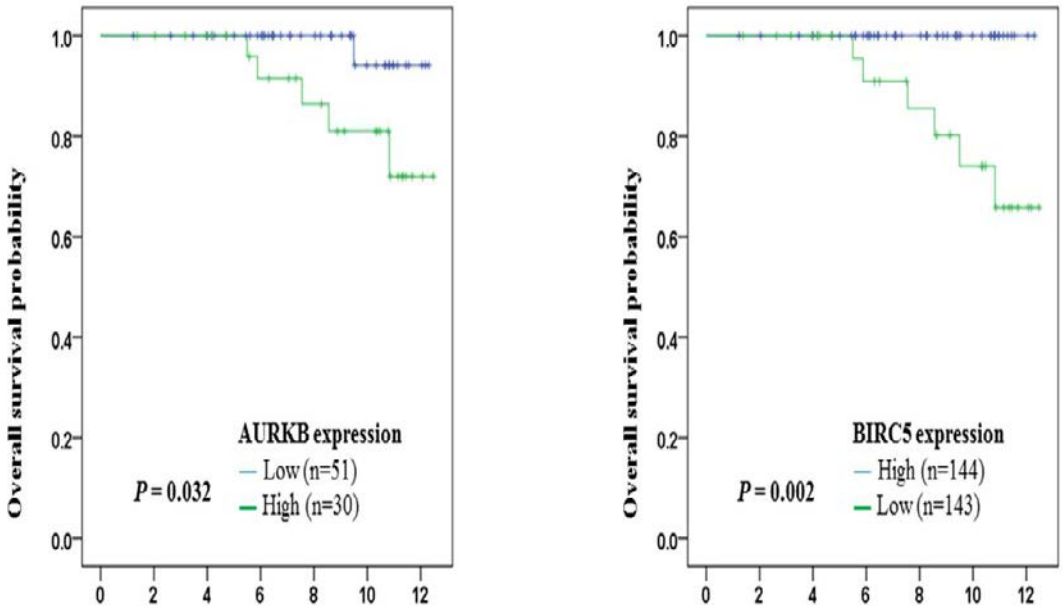

Figure 2

FP05-4

STANDARDIZATION OF KI67 ASSESSMENT FOR EFFICIENT USE OF THE ONCOTYPE DX ASSAY IN BREAST CANCER PATIENTS

Yoshio Mizuno[1], **Hiromi Fuchikami**[1*], **Naoko Takeda**[1*], **Junichi Yamada**[2*], **Hiroaki Abe**[2*], **Kazuhiko Sato**[1*]

[1] *Dept. of Breast Oncology, Tokyo-West Tokushukai Hospital, Japan*
[2] *Dept. of Clinical Pathology, Tokyo-West Tokushukai Hospital, Japan*

Background/Purpose : The assessment of the nuclear antigen Ki67 has been widely investigated as a predictive and prognostic marker for early breast cancer, but till date, there is no standard Ki-67 assessment method. On the other hand, the use of the Oncotype DX assay has increased worldwide, but it is very expensive and the National Health Insurance program in Japan does not cover this cost. Therefore, we need to use this assay more efficiently by selecting appropriate patients. In this retrospective study, we compared the Oncotype DX recurrence scores (RS) between non-standardized and standardized Ki67 assessments to reconsider an addition of chemotherapy to hormonal therapy.

Methods : The Oncotype DX assay was performed in 21 patients with early breast cancer (T1-2, N0-1mi, M0, estrogen receptor-positive, human epidermal growth factor receptor 2-negative) from December 2011 to February 2013. When the progesterone receptor (PgR) status was introduced during the classification of intrinsic subtypes, 8 patients were classified as luminal B subtype (PgR <20%). The 13 other patients were categorized using the Ki-67 assessment method by both local pathologists and a central review. If Ki-67 was >14%, we considered chemotherapy as an adjuvant therapy. The correlation between RS categories generated by the Oncotype DX assay and intrinsic subtypes based on Ki-67 labeling index (LI) using standardized and non-standardized methodologies was evaluated.

Results : The median patient age was 56 years (range, 36-80 years), tumor size was 1.6 cm (range, 0.5-3.0 cm), Ki-67 LI with non-standardized method was 9 (range, 2-33), and RS was 17 (range, 6-30). Of the 8 patients with luminal B subtype (PgR <20%), 7 (87.5%) were moderate to high risk (RS ≥18). In the other 13 patients, 11 were low risk (RS <18) and only 2 were moderate risk (RS range, 18-30). We categorized these 13 patients by Ki-67 LI; 10 showed a high Ki-67 (>14%) after evaluation by local pathologists, but only one showed a high Ki-67 after evaluation by central review. If we used the Ki-67 LI which was evaluated by local pathologists, 76.9% (10/13) patients with high PgR status should be considered for treatment including chemotherapy. However, if we used the Ki-67 LI, which was evaluated by central review, only 7.7% (1/13) patients with high PgR status should be considered for treatment including chemotherapy.

Conclusion : In this study, we found that in patients with high PgR status (≥20%), the Ki-67 LI which was evaluated by the central review showed lower values than that evaluated by local pathologists. Furthermore, for those evaluated by the central review, the incidence of including chemotherapy was notably decreased. The results showed that if standardized Ki-67 assessment is not possible, the Oncotype DX assay should be used to determine whether chemotherapy should be included. These results suggested that it is important to use standardized Ki-67 assessment for selection of appropriate patients for the Oncotype DX assay.

FP05-5

CLINICAL USEFULNESS OF AUTOMATED ASSESSMENT OF KI-67 PROLIFERATIVE ACTIVITY USING A PUBLIC DOMAIN IMAGE ANALYSIS SOFTWARE, IMMUNORATIO

Ahwon Lee[1*], Hee Eun Kim[1], Byung Joo Chae[2], Byung Joo Song[2], Sang Seol Jung[2], Min-Kyung Yeo[1]

[1] *Dept. of Hospital Pathology, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*
[2] *Dept. of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*

Background/Purpose : Immunohistochemical assessment of Ki-67 is an established prognostic factor in breast cancer. To use Ki-67 labeling index in routine clinical practice, standardized and easily assessable interpretation method is necessary.

Methods : We immunohistochemically assayed proliferation activity of operable BC in 577 patient who underwent surgical resection between January 2003 and January 2007. Ki-67 immunostaining was performed on 2.0 mm core tissue microarray (TMA) and then the labeling index (LI) was manually counted using image processing program (Adobe Photoshop). We re-evaluated the Ki-67 labeling index using ImmnoRatio, a publicly accessible web based image analysis software.

Results : Mean value of Ki-67 LI was 24.4 ± 19.8 by manual count and 20.3 ± 18.2 using ImmunoRatio, respectively. Manual Ki-67 LI and ImmunoRatio Ki-67 LI are well correlated (Pearson correlation= 0.97 and P value<0.001). Using 20% cut-off of Ki-67 LI, the concordance rate between manual and ImmunoRatio Ki-67 was excellent (kappa coefficient=0.881). On univariate analysis, both manual and ImmunoRatio high Ki-67 LI were associated with poor breast cancer specific survival (p=0.019 and p=0.038, respectively). Among hormone receptor positive subgroup, both manual and ImmunoRatio high Ki-67 LI were associated with poor breast cancer specific survival (p=0.022, each), in contrast to hormone receptor negative subgroup, in which, both manual and Immunoratio high ki-67 LI were not associated with poor breast cancer specific survival (p=0.955 and p=0.544, respectively).

Conclusion : The Ki67 LI acquired using free web based software, ImmunoRatio, was highly correlated with manual Ki-67 LI acquired using image processing software, Adobe Photoshop. With the cut-point of 20%, both manual and ImmnoRatio high Ki-67 LI were poor prognostic factor, especially in hormone receptor positive subgroups.

FP05-6

A ROLE OF BREAST DENSITY AS A PROGNOSTIC FACTOR FOR LATE DISTANT METASTASIS IN PREMENOPAUSAL, HORMONE RESPONSIVE/HER2 NEGATIVE BREAST CANCER PATIENTS AFTER COMPLETION OF 5 YEARS OF ADJUVANT THERAPY

Guiyun Sohn, Jong Won Lee*, Yura Lee, Hee Jung Kim, Beom Seok Ko, Jong Han Yu, Byung Ho Son, Sei Hyun Ahn

Dept. of Surgery, ASAN Medical Center, Korea

Background/Purpose : Background: This study aims to confirm a prognostic value of breast density (BD) for late distant metastasis according to breast cancer subtypes.

Methods : Methods: This study included 1,401 breast cancer survivors identified from web-based database of Asan Medical Center. All patients were diagnosed as breast cancer from 2001 to 2003 and free of recurrence or metastasis at the time of 5 year follow-up. Breast density (Percent density, PD) was calculated using a computer-assisted thresholding method, Cumulus TM from digital mammogram of a cancer-free breast after completing 5 years of various adjuvant treatments. Late distant metastasis was defined as distant metastasis after 5 years from initial operation. All patients were grouped according to their hormone receptor and HER2 subtypes: HR+ and HER2-; HR+ and HER2+; HR- and HER2+; and HR- and HER2- subtypes. Distant metastasis free survival (DMFS) was estimated by the Kaplan-Meier method. Log-rank tests were used for the comparison of survival curves. Multivariate analyses were performed using Cox's proportional hazard regression model.

Results : Results: The median follow-up was 113 months. In the HR+/HER2- subtype, late DMFS was associated with higher PD (middle third vs. lower third; log-rank p=0.033) along with younger age (<40 vs. ≥40 years); larger tumor size (>2 cm vs. ≤2 cm); positive lymph node (LN) metastasis; higher nuclear grade; and immunohistochemical p53 positivity (log-rank p=0.004; 0.009; 0.006; 0.033; and 0.061, respectively). In a multivariate analysis including body mass index, higher PD had a borderline significance (hazard ratio=6.87, p=0.075). Younger age, positive LN metastasis, and p53 positivity were independent prognostic factors for DMFS (hazard ratio/p value=6.63/0.004; 6.64/0.013; and 4.03/0.024, respectively).

Conclusion : Conclusion: Higher breast density after completion of 5 years of adjuvant therapy can be a complementary prognostic factor for late distant metastasis in addition to traditional prognostic factors in HR+/HER2- invasive breast cancer.

FP05-7

IMPACT OF INITIAL SURGICAL TREATMENT DELAY ON SURVIVAL ACCORDING TO HORMONE RESPONSIVENESS IN BREAST CANCER

Tae-Kyung Yoo, Wonshik Han*, Hyeong-Gon Moon, Jisun Kim, Jun Woo Lee, Min Kyoon Kim, Eunshin Lee, Jongjin Kim, Dong-Young Noh

Dept. of Surgery, College of Medicine, Seoul National Univ., Korea

Background/Purpose : Previous studies on the issue of the prognostic importance of treatment delay in breast cancer have shown inconsistent results. Furthermore, the association between the impact of treatment delay and molecular characteristics of tumors has not been adequately addressed. The purpose of this study is to examine the prognostic impact of initial surgical treatment delay after biopsy-proven cancer diagnosis in breast cancer patients.

Methods : A total of 1,201 consecutive invasive breast cancer patients, treated in Seoul National University Hospital, Seoul, Korea, between July 2006 and June 2008, were included in this study. Patients with in situ or metastatic carcinoma at the time of diagnosis, patients who received other treatment than surgery as initial treatment, and patients in whom the dates of the initial pathologic diagnosis were unknown were excluded.

Results : The median time fro biopsy-confirmed cancer diagnosis to initial surgical treatment was 25 days (range 0-134). When the patients were classified according to their treatment delay days (0 - 29 days, 30 - 59 days, and ≥ 60 days), there was no difference in survival between '0-29 days' group and '30-59days' group. However, for patients who experienced more than 60 days of initial delay in surgical treatment (n=26, 2.2%), the survival was significantly worse when compared to other groups (p=0.034). The association between treatment delay and poor outcome was only seen in patients with ER and PR negative tumors (p=0.018) while patients with hormone-responsive tumors showed no such association. Patients with ER and PR negative tumors developed more recurrence and had shorter disease-free survival if they had treatment delay of more than 60 days (p=0.018). The prognostic importance of treatment delay of more than 60 days remained significant in predicting overall survival (OS) and disease-free survival (DFS) after adjusting for other known prognostic factors such as age, tumor size, nodal status and nuclear grade (OS: HR 11.136: 95% CI 2.170 - 57.148, p=0.004; DFS: HR 6.098, 95% CI 1.791 - 20.765, p=0.004).

Conclusion : Our results suggest that having treatment delay of more than 60 days is associated with poor treatment outcome in patients with ER and PR negative breast cancer.

FP05-8

MALIGNANT PHYLLODES TUMOR OF THE BREAST: CLINICAL OUTCOMES OF PATIENTS TREATED WITH SURGERY AND RADIOTHERAPY

Jihye Cha[1], **Joohwan Lee**[2], **Yong Bae Kim**[2], **Ki Chang Keum**[2], **Seung Il Kim**[3], **Byeong Woo Park**[3], **Chang-Ok Suh**[2*]

[1] *Dept. of Radiation Oncology, Wonju College of Medicine, Yonse Univ., Korea*
[2] *Dept. of Radiation Oncology, College of Medicine, Yonsei Univ., Korea*
[3] *Dept. of Surgery, College of Medicine, Yonsei Univ., Korea*

Background/Purpose : Malignant phyllodes tumor is very rare and its standard treatment is wide excision with histologically negative margin. The objective of this study was to evaluate the outcome of surgery and radiotherapy for malignant phyllodes tumor of the breast and describe the patterns of failure.

Methods : We retrospectively reviewed all malignant phyllodes tumor patients who had radiotherapy to the breast after surgery between January 1990 and December 2012 at our institution. Ten patients were identified: nine patients were female and one patient was male. The male patient was lost to follow up right after the completion of radiotherapy and excluded from the analysis. Data on characteristics of patients, histologic features, treatment details, recurrence, and status at follow-up were analyzed.

Results : Median age of the patients was 46. Two patients (22%) had previous history of benign phyllodes tumor. Six patients (67%) underwent partial mastectomy or wide excision and total mastectomy was performed to 3 patients (33%). Four patients (44.5%) had axillary lymph node dissection. A patient number of T1, T2, and T3 was one (11%), four (44.5%), and four (44.5%), respectively. None of the patients showed histology-proven lymph node metastasis. Close surgical margins <1 cm were found in 3 patients (33%). The aim of radiotherapy was postoperative after first surgery, postoperative after salvage surgery and palliative in seven (78%), one (11%), and one patient (11%), respectively. Median dose to the tumor bed and breast was 55 and 50 Gy, respectively. Only one patient received 50.4 Gy of radiotherapy to regional lymph node area. Neoadjuvant and adjuvant chemotherapy was done in one patient and three patients, respectively. Two patients died of the disease and 5-year overall survival rate was 78%. Both patients had initial T3 disease and developed distant metastases during their disease course. One of them received radiotherapy to the breast area after lung metastasis developed. Close surgical margins < 1 cm (p=0.027) and necrosis (p=0.008) were significant factors for worse overall survival. During the follow-up period of six patients who received radiotherapy after the initial surgery, local failure was observed in only one patient. She had nipple sparing mastectomy, adjuvant chemotherapy and radiotherapy, but she experienced T4 recurrence. Despite the salvage surgery and target agent therapy, her disease progressed and finally she had pleural, cardiac, mediastinal and retroperitoneal lymph node metastasis and expired. There was no regional failure observed in our series.

Conclusion : Radiotherapy following surgical resection resulted in good local control for malignant phyllodes tumor. Close margin < 1 cm and tumor necrosis seems to be poor prognostic factors affecting overall survival.

GBCC2013

Poster Discussion

PO01-01

DEVELOPMENT OF MODEL FOR PREDICTING BRCA1 AND BRCA2 MUTATIONS IN KOREAN BREAST CANCER PATIENTS: KOHBRA BRCA RISK CALCULATOR (KOHCAL)

Eunyoung Kang[1], **Sung-Won Kim**[1*], **Sue K. Park**[2], **Min Hyuk Lee**[3], **Sei-Hyun Ahn**[4], **Korean Hereditary Breast Cancer Study Group**[5]

[1] *Dept. of Surgery, Seoul National Univ. Bundang Hospital, Korea*
[2] *Dept. of Preventive Medicine, College of Medicine, Seoul National Univ., Korea*
[3] *Dept. of Surgery, Soonchunhyang Univ. Hospital, Korea*
[4] *Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*
[5] *Korean Breast Cancer Society, Korea*

Background/Purpose : Previous study showed that widely used BRCA risk prediction models, the BRCAPRO and Myriad II, underestimated the number of mutation carriers in Korean breast cancer patients. Therefore, these Western models are not appropriate for determining eligibility for *BRCA* mutation genetic testing in Korean population. Our aim was to identify predictive factors for *BRCA*1/2 mutations, and to develop Korean BRCA risk calculator.

Methods : Through the Korean Hereditary Breast Cancer Study, 1677 female patients who were enrolled between May 2007 and Dec 2010 were used for model construction. Logistic regression model was used to determine the predictive factors for positive *BRCA*1/2 mutations and to develop model for prediction of mutation probability. A separate dataset of 402 patients who were enrolled from Jan 2011 to August 2012 was used to test performance of our model.

Results : A total of 261 *BRCA* mutation carriers (15.8%) were identified among model set. In multivariate logistic models, age at diagnosis of breast cancer, bilateral breast cancer, triple-negative breast cancer, and number of relatives with breast or ovarian cancer were independent factors for a *BRCA* mutation among familial breast cancer patients. Among non-familial breast cancer patients, age at diagnosis of breast cancer <35 years, bilateral breast cancer, both breast and ovarian cancer, and triple-negative breast cancer remained as significant predictive factors. Korean BRCA risk calculator was developed based on logistic regression models and beta coefficients for each variable. As a result of validation, there were no differences between the observed carrier proportions and the expected carrier probabilities within each threshold categories. At 10% estimated probability, our model for familial breast cancer had very high sensitivity.

Conclusion : We developed Korean BRCA risk calculator based on personal and family history of breast and ovarian cancer and pathologic characters. Our model will be a useful tool to provide appropriate genetic risk assessments for Korean population.

PO01-02

AFFECTING FACTORS TO UPTAKE *BRCA*1/2 GENETIC TESTING IN HIGH-RISK FAMILIES FOR HEREDITARY BREAST AND OVARIAN CANCER

Young Sun[1], **Eunyoung Kang**[1], **Dongwon Kim**[2], **Euijun Hwang**[1], **Jaehag Jung**[1], **Cha Kyong Yom**[1], **Sung-Won Kim**[1]

[1] *Dept. of Surgery, College of Medicine, Seoul National Univ. Bundang Hospital, Korea*
[2] *Dept. of Surgery, Daerim Saint Mary's Hospital, Korea*

Background/Purpose : Individuals with a risk of hereditary breast and ovarian cancer face the decision whether to obtain *BRCA* genetic testing. The purposes of our study are to determine the rate of obtaining genetic testing and the reasons of non-uptake, and to identify the factors affecting uptake of *BRCA* genetic testing in high risk patients

Methods : We identified 804 individuals who had genetic counseling for *BRCA*1/2 mutation in Seoul National University Bundang Hospital from July 2003 to September 2012. The genetic counseling was performed for the 647 breast cancer patients who were the target of the testing. For families, information was given through the patients who have been identified as *BRCA* mutation carrier. And when wanted, the genetic counseling was performed. In case of the families, because the genetic counseling was done for only those who had decided to undergo the testing, 100% testing was undertaken for 157 (18.9%) participants.

Results : In total, 571(88.2%) patients decided to be tested for *BRCA*1/2 mutation after the genetic counseling. The mean age of persons who had the genetic testing was significantly younger than those of persons who did not (43.2 vs. 45.8 years old, p=0.058). The rate of uptake of genetic testing in patients with less than 40 years old (91.1%) was significantly higher than that in patients with more than 40 years old (84.8%, p=0.014). In multivariate analysis, the family history of breast cancer showed to be a independent variable (OR=1.963, 95% CI=1.024-3.764, p=0.042). Also, the age with 40 or less than 40 years old was a independent variable (OR=3.205, 95% CI=1.550-6.622, p=0.002). In 132 persons with initial non-uptake genetic testing, 58 (43.9%) postponed the decision. 30 (22.7%) needed time to discuss with family members and 22 (16.7%) did not want to know whether there is *BRCA*1/2 mutation. 22 (16.7%) refused the test because of financial problems. The fifty-six (42.4%) patients who refused initially underwent the testing later on. When dividing the individuals who refused the genetic test due to financial hardship by before and after National health insurance coverage, 11 out of 18 (61.1%) refusals were due to financial difficulty before the coverage. However, only 11 out of 114 (9.6%) refused with financial reason after the insurance coverage

Conclusion : In our institution, the rate of obtaining *BRCA* genetic testing was comparatively high. The family history of breast cancer and age with 40 or less than 40 years-old was the important factor associated with uptake of genetic testing. More than 40% of initially non-uptake persons had genetic testing, so follow up of them is important. National health insurance decreased the proportion of financial reason in non-uptake persons. In genetic counseling, we have to understand these issues and consider several factors that may influence the individual's decision.

PO01-03

PREVALENCE OF BRCA1/2 MUTATIONS IN HIGH-RISK INDIVIDUALS FOR HEREDITARY BREAST AND OVARIAN CANCER IN KOREA : THE KOREAN HEREDITARY BREAST CANCER STUDY (KOHBRA STUDY)

Young Sun[1], **Eunyoung Kang**[1], **Sung-Won Kim**[1*], **Min Hyuk Lee**[2], **Sei Hyun Ahn**[3], **Sue K. Park**[4], **Korean Hereditary Breast Cancer Study Group**[5]

[1] *Dept. of Surgery, College of Medicine, Seoul National Univ. Bundang Hospital, Korea*
[2] *Dept. of Surgery, Soonchunhynag Univ. Hospital, Korea*
[3] *Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*
[4] *Dept. of Preventive Medicine, College of Medicine, Seoul National Univ., Korea*
[5] *Korean Breast Cancer Society, Korea*

Background/Purpose : In 2007, the Korean Hereditary Breast Cancer Study (KOHBRA Study) started to estimate the prevalence of *BRCA*1/2 mutations among a high-risk group of patients with hereditary breast cancer and their families and to establish a *BRCA* carrier cohort to identify the natural history of hereditary breast and ovarian cancer in Korea.

Methods : The KOHBRA Study is a prospective multicenter cohort identifying cases and their families. More than 3000 subjects from 40 centers participated in this study, and all participants received genetic counseling and *BRCA* genetic testing. The clinical information and blood samples for banking were collected. The analysis of the prevalence of *BRCA*1/2 mutations was determined from 2794 patients who were enrolled between May 2007 and August 2012.

Results : In total, 390 mutation carriers among 2302 index patients were identified (*BRCA*1, 153; *BRCA*2, 232; both *BRCA*1 and *BRCA*2, 5). The prevalence of the *BRCA* mutation was as follows: 24.5% (282/1152) for breast cancer patients with a family history of breast/ovarian cancers; 7.5% (62/826) for patients with early-onset (≤40 years) breast cancer without a family history; 13.0% (18/138) for patients with bilateral breast cancer; male breast cancer in 5.0% (1/20); and 20.0% (1/5) for patients with breast and ovarian cancer; 22.0% (24/109) for patients who have two or more high risks without a family history. From the analysis of the mutation characteristics, 62 different *BRCA*1 and 35 *BRCA*2 mutations were identified. The 7708C>T (p.Arg2494X) mutation in *BRCA*2 (11.0%) was most commonly identified.

Conclusion : The KOHBRA Study is the largest prospective cohort study to identify *BRCA* mutation carriers in Asia. The results of this study suggest that the prevalence of *BRCA* mutations in Korean subjects is similar to the prevalence reported among Western cohorts. These findings will be the baseline data for the genetic counseling and the genetic test in Korean populations.

PO01-04

THE NATIONWIDE SURVEY FOR THE PRACTICE PATTERNS OF MANAGING HEREDITARY BREAST AND OVARIAN CANCER IN KOREA

Eunyoung Kang[1], Sung-Won Kim[1*], Min Hyuk Lee[2], Sei-Hyun Ahn[3], Sue K. Park[4], Korean Hereditary Breast Cancer Study Group[5]

[1] *Dept. of Surgery, Seoul National Univ. Bundang Hospital, Korea*
[2] *Dept. of Surgery, Soonchunhyang Univ. Hospital, Korea*
[3] *Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*
[4] *Dept. of Preventive Medicine, College of Medicine, Seoul National Univ., Korea*
[5] *Korean Breast Cancer Society, Korea*

Background/Purpose : Before and after the Korean Hereditary Breast Cancer Study (KOHBRA Study), in the 2007 and 2009, we performed surveys to examine practice patterns of hereditary breast and ovarian cancer (HBOC) in Korea. From the surveys, we noticed that the KOHBRA Study has an important role in clarifying the proper process and selecting appropriate candidates for genetic testing. Through the KOHBRA Study, about 3200 patients at high risk for HBOC and their families from 40 centers received genetic counseling and testing between May 2007 and April 2013, and a change in practice patterns of HBOC is expected. Therefore, we performed a nationwide survey to examine the changed patterns for the management of HBOC.

Methods : The survey was performed using the identical questionnaire to the previous surveys from 5th to 25th in June 2013. Centers which belong to the Korean Breast Cancer Society were invited to participate in the survey by e-mail. A total of 35 centers responded to the survey.

Results : In total institutions, 97.1% (34/35) asked for family history of cancer to patients with breast cancer and 54.3% (19/35) draw a pedigree. All institutions had *BRCA*1 and *BRCA*2 genetic testing codes and recommended genetic testing for patients with risk of HBOC. The answer to the question of a *BRCA* genetic testing indication was as follows: breast cancer patients with family history of breast or ovarian cancer (100%), early-onset (< 40 years) (91.4%), bilateral breast cancer (91.4%), male breast cancer (80.0%), and multiple cancers (45.7%). Twenty eight of 35 institutions (80.0%) provided genetic counseling before their patients underwent a genetic test. Genetic counseling was provided by doctors (65.7%), genetic counselors (8.6%), or KOHBRA Study research assistants (17.1%). Among 26 institutions, 825 *BRCA*1/2 mutation carriers of 606 families have been identified. Chemoprevention by tamoxifen and oral pill were recommended for *BRCA*1/2 mutation carriers in 9 and 3 of 26 centers, respectively. Only 9 unaffected carriers were actually managed by tamoxifen. Bilateral prophylactic mastectomy, contralateral prophylactic mastectomy, and prophylactic oophorectomy were recommended in 12, 8 and 15 of 26 centers, and actually performed in 2, 17 and 117 carriers, respectively.

Conclusion : Nowadays, most of institutions in Korea provide a pre-test genetic counseling before genetic test and a *BRCA* genetic testing candidate are selected more appropriately than in the previous surveys. For management for *BRCA*1/2 mutation carriers, chemoprevention and risk-reducing surgery for breast and ovarian cancer prevention are not widely performed in Korea.

PO01-05

THREE NEW CAUSATIVE POTENTIAL LOCI OF CANDIDATE GENES: A GENOME-WIDE ASSOCIATION STUDY OF BREAST CANCER IN INDONESIA SUB-POPULATION

Samuel Johny Haryono[1*], Teguh Aryandono[2*], Kartika Sari[3*], Raymond Mulyarahardja[3], I Gusti Bagus Datasena[3]

[1] *Dept. of Oncology, Dharmais National Cancer Institute; MRCCC Siloam Hospital; Jakarta VIVO Research Initiatives, Indonesia*

[2] *Dept. of Oncology, Faculty of Medicine Gajah Mada Univ., Indonesia*

[3] *Dept. of Oncology, MRCCC Siloam Hospital; Jakarta VIVO Research Initiatives, Indonesia*

Background/Purpose : It has been generally accepted that breast cancer is the most heterogeneity cancer, driven by genetic changes and environment factors. However, hereditary susceptibility factor has recently been an issue in Asian region, several researches have been collaboratively conducted for searching the causative candidate genes

Methods : A microarray base of Genome-Wide Association Study (GWAS) was performed. Having 443.821 SNPs from blood samples of 89 cases and 46 controls of sub-population in Java, Indonesia SNPs analysis was conducted employing Genotyping Console, Plink, and Haploview.

Results : We identified 4 new susceptibility loci, IQSEC3 on 12p13.33 (rs6489190,P=$1.8x10^{-7}$, odds ratio [OR]=0,1764), ZNF595 and ZNF718 on 4p16.3 (rs7673078, p=$8.2x10^{-6}$, OR=0.1275; rs2111836, p=$1.6x10^{-5}$, OR=3,784; rs10014562, p=$2.6x10^{-5}$, odds ratio OR= 0.021), and FAM110C on 2p25.3 (rs13025833, p=$2.6x10^{-5}$, OR=0.3289; rs873159 (p=$2.7x10^{-5}$), OR=0.1683). The entire 31 SNPs that shows a promising significant value will be replicated on the second stage of the study, rs6489190 (p=$1.8x10^{-7}$), rs11629756 (p=$6.9x10^{-6}$), rs7673078 (p=8,2x10-6), rs2112460 (p=$8.2x10^{-6}$), rs131031 (p=$8.2x10^{-6}$), rs1948097 (p=$1.3x10^{-5}$), rs11950065 ($1.4x10^{-5}$), rs35675336 ($1.4x10^{-5}$), rs41406347 ($1.4x10^{-5}$), rs2111836 (p=$1.6x10^{-5}$), rs8087976 (p=$1.6x10^{-5}$), rs11784296 (p=$1.9x10^{-5}$), rs4770892 (p=$2x10^{-5}$), rs6856348 (p=$2.5x10^{-5}$), rs341731 (p=$2.6x10^{-5}$), rs10014562 (p=$2.6x10^{-5}$), rs332757 (p=$2.6x10^{-5}$), rs13025833 (p=$2.6x10^{-5}$), rs873159 (p=$2.7x10^{-5}$), rs10752589 (p=$3.4x10^{-5}$), rs6888813 (p=$3.4x10^{-5}$), rs6887937 (p=$3.5x10^{-5}$), rs988031 (p=$4x10^{-5}$), rs4451902 (p=$4x10^{-5}$), rs4922060 (p=$4x10^{-5}$), rs1383966 (p=$4.3x10^{-5}$), rs7812985 (p=$4.3x10^{-5}$), rs7828156 (p=$4.5x10^{-5}$), rs1383965 (p=$4.6x10^{-5}$), rs1000769 (p=$4.9x10^{-5}$), rs10984339 (p=$5x10^{-5}$).

Conclusion : This Identification and further searching of the candidate genes with their loci in Asian hereditary susceptibility breast cancer will give continuous contribution in collecting the gene variants, and provide the genetic test option for breast cancer risk assessment and cancer prevention program among Asian women.

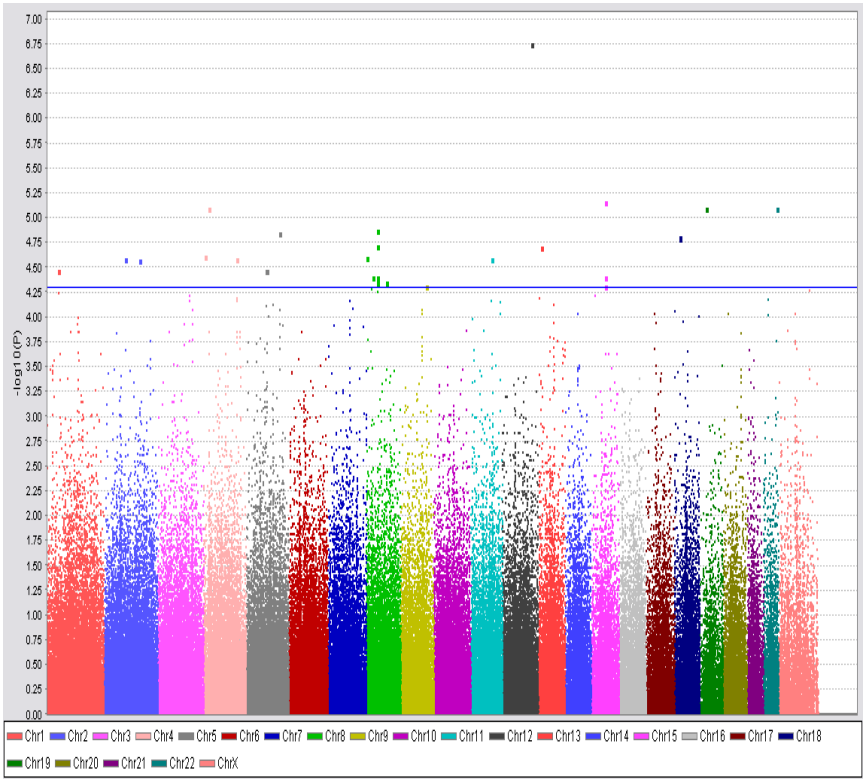
-log10(P)
Chr1 Chr2 Chr3 Chr4 Chr5 Chr6 Chr7 Chr8 Chr9 Chr10 Chr11 Chr12 Chr13 Chr14 Chr15 Chr16 Chr17 Chr18
Chr19 Chr20 Chr21 Chr22 ChrX

Figure 1

PO01-06

KNOWLEDGE, ATTITUDES, AND INTENTION TOWARD GENETIC TESTING IN BREAST CANCER PATIENTS WITH HIGH RISK OF HEREDITARY BREAST CANCER

Hye Mi Park[1], **Sang-Eun Jun**[2*]

[1] *Breast Cancer Center, Chilgok Kyungpook National Univ. Medical Center, Korea*
[2] *College of Nursing, Keimyung Univ., Korea*

Background/Purpose : The purpose of this study was to investigate knowledge about the hereditary breast cancer (HBC), attitudes about genetic testing for breast-ovarian cancer susceptibility and intention towards having genetic testing in breast cancer patients with high risk of HBC.

Methods : One hundred eight women with breast cancer who were diagnosed before 40 years of age were recruited. Knowledge was assessed with a 20-item true-false scale and attitudes were measured with 16 Likert-style items (1 'strongly disagree' to 5 'strongly agree') which consisted of 8 pros and 8 cons. One question was used to ask their intention to have a genetic test and responses were 'definitely yes', probably yes', 'considering test' and 'not interested'.

Results : The percentage of subjects responded correctly to individual knowledge items ranged from 9% to 94%. For instance, 92% of the subject knew that women who do not have a mutated gene can still get cancer and 71% were aware that all women who have an altered gene may not get cancer. However, 11% of the subjects were knowledgeable about the prevalence of *BRCA* 1 mutations and 32% knew the proportion of breast cancer cases attributable to the *BRCA*1 gene. A positive attitude toward obtaining a genetic test was predominated. The benefit of genetic testing rated as most important was "to help my daughters or sisters decide whether to undergo genetic testing" (rated by 97% of subjects) and "to motivate me to perform breast self-examination more frequently" (rated by 94%). The most important perceived limitation was "If I were found to carry the gene, it would jeopardize my insurance coverage or lead to problems with my employers" (rated by 56%). If a genetic test were made available, 40% of the subjects indicate that they would definitely/probably have it and 48% answered they would consider it.

Conclusion : These results provided that breast cancer patients with high risk of HBC understand some important facts about the inheritance of breast cancer and genetic testing. Although subjects' knowledge about the genetics of breast cancer was limited, their interest in genetic testing was substantial. Considering previous reports that perceptions of the benefits of genetic testing were important predictors of *BRCA*1 test utilization, the developments of educational strategies and counseling programs to deliver proper knowledge are needed.

PO01-07

THE IMPACT OF APOCRINE METAPLASIA ON NEWLY DEVELOPED LESION AT VACUMN ASSISTED BREAST BIOPSY SITE

Dong Won Ryu

Dept. of Breast Surgery, Kosin Univ. Gospel Hospital, Korea

Background/Purpose : Recently FDA approved use of this instrument for therapeutic purpose of benign lesions. We also used the instruments for therapeutic purpose for benign lesions. But we sometimes experienced the tumor regrows that previous MMT site or adjacent tissue. We wanted to evaluate the factors that impact on remained or tumor regrowth at post biopsy site or adjacent tissue. Especially our study focused on apocrine metaplasia and hyperplastic diseases' influence in tumor re-growth.

Methods : From January 2000 to December 2012, we could analyze 952 cases because of follow up. Median follow up period of the patients was 11 months. The patient age at initial diagnosis, the age of menarche, status of marriage, the number of babies, presence or absence of feeding Hx, status of menopause, presence or absence of family history were obtained from medical records Tumor size, pathologic diagnosis, presence or absence of calcification were obtained from pathology reports. The chi-squared test was used to evaluate correlation between apocrine metaplasia and clinicopathologic parameters in all cases A p-value of <0.05 was considered to indicate statistical significance DFS was defined as time to any type of recurrence at tumor site or adjacent tissue.

Results : In our study Mean age is 46.29 years old. And mean BMI was 25.20. About 16.5% (n=157) cases has belongs to apocrine metaplasia. The number of tumor that had 5-10mm tumor size was 301 (31.5%) cases. Apocrine metaplasis was diagnosed in 16.5% (n=157). And Severe ductal hyperplasia was 0.6% (n=6). tumor recurrence rate was 1.5% (n=15). Regrowth rate in severe ductal hyperplasia was 50% (3/6), in papilloma was 2.1% (1/46) and in Apocrine metaplasia was 5.1% (8/157). Apocrine dysplasia, apocrine metaplasia were not significantly associated with tumor regrowth at post vacumm assisted breast biopsy (VABB) site. Additionally tumor with more than 10mm tumor size and severe (florid) ductal hyperplasia were significantly associated with tumor regrowth at post VABB site.

Conclusion : Apocrine metaplasia were not significantly associated with tumor regrowth at post VABB site.

PO01-08

A COMPARATIVE STUDY ON KNOWLEDGE, ATTITUDE, AND PREVENTIVE BEHAVIORS CONCERNING CANCER BETWEEN MIDDLE-AGED KOREAN AND KOREAN-CHINESE

Ying Hua Cui, Jeong Sook Park, Kyung Hee Lim*

College of Nursing, Keimyung Univ., Korea

Background/Purpose : The purpose of this study was to compare knowledge, attitude and preventive behaviors concerning cancer between middle-aged Korean and Korean-Chinese, and to provide basic data for developing health education and promotion programs with a cultural perspective.

Methods : The subjects of this study consisted of 140 Korean who were living in D city, Korea and 150 Korean-Chinese who were living in Y city, China. Data were collected from October 6, 2011 to October 14, 2011 using a self-reported questionnaire. Descriptive statistics, t-test, and ANOVA were used for data analysis using SPSS 19.0 program.

Results : The Korean subjects showed significantly higher score than the Korean-Chinese subjects in terms of knowledge on cancer ($t=-3.88$, $p<0.001$). In contrast, the Korean-Chinese subjects showed significantly higher score than the Korean subjects in attitude towards cancer ($t=2.80$, $p=0.005$) and preventive behavior concerning cancer ($t=3.06$, $p=0.002$). Regarding knowledge of cancer, Korean (80.8%) and Korean-Chinese (88.4%) showed the highest percentage of correct answers on general characteristics of cancer and the lowest percentage of correct answers on cervical cancer. In the attitude of cancer, both groups showed the highest score in the benefit domain and the lowest score in the barrier domain. Regarding preventive behaviors for cancer, the Korean subjects reported the highest score on healthy sexual life and Korean-Chinese showed the highest score on diet of fruits and vegetables. Both groups showed the lowest score on regular exercise.

Conclusion : This research showed that Koreans had a lot of knowledge about cancer, but they were passive to perform preventive behaviors for cancer. Therefore, it is necessary to develop cancer preventive programs for them to easily participate. For Korean-Chinese, it is imperative to develop educational programs to improve their knowledge of cancer.

PO01-09

INVESTIGATION ON THE ASSOCIATION BETWEEN BREAST CANCER AND CONSUMPTION OF COMBINED ORAL CONTRACEPTIVE PILLS IN WOMEN

Fariba Taleghani[1*], **Sohila Ehssanpour**[1], **Fahimeh Sayed Ahmadinejad**[1], **Fariborz Mokarian**[2]

[1] *Nursing & Midwifery Care Research Center, Isfahan Univ. of Medical Sciences, Iran*
[2] *Dept of. Hematology Oncology, School of Medicine, Isfahan Univ. of Medical Sciences, Iran*

Background/Purpose : Oral contraceptive pills are among the most popular contraceptive methods, but the fear of cancer and cardiovascular disease overshadows its continuous use among women. This study aimed to define the association between consumption of combined oral contraceptives among women with breast cancer.

Methods : This is an analytical case- control study conducted on 175 women with breast cancer referring to a cancer hospital and private clinics in Isfahan to be treated as well as 350 healthy women who were identical with the subjects in the study group regarding age and residential location. The data were collected by a researcher made questionnaire which contained four sections for the study group and three sections for the control. The data were collected by reviewing and observation of documented evidences as well as interviews. Content validity and Chronbach's alpha were employed to confirm validity and scientific reliability of the questionnaire respectively. The data were analyzed by descriptive and analytical statistical methods through SPSS ver18.

Results : The findings showed that there was a significant association between history of contraceptive pills consumption and incidence of breast cancer ($p<0.001$). There was no significant association between duration of use, age of the first and the last use, and time since the first and the last use in study and control groups($p>0.05$). Pills consumption was significantly higher in the invasive lobular breast cancer (n=5, 52%) compared to invasive lobular breast cancer (n=7, 40%) ($p<0.001$), multivariable regression analysis shown family history of breast cancer increased the risk of breast cancer by 3.88 folds, oral contraceptive use increased by 2.17 folds, academic education increased by 1.23 folds.

Conclusion : The results showed that history of contraceptive pills consumption is associated with incidence of breast cancer and histological type.

PO01-10

A STUDY ANALYSING B2 CORE BIOPSIES THAT SUBSEQUENTLY DEVELOPED BREAST CARCINOMA

Hassaan Qaiser Sheikh[1], **Tahir Masudi**[2*], **Vidya Kumaraswamy**[3], **Shabana Iqbal**[4], **Alison Waterworth**[4], **Narinder Sharma**[4], **Vijay Modgill**[4]

[1] *Dept. of General Surgery, Calderdale and Huddersfield NHS Foundation Trust, United Kingdom*
[2] *Dept. of Breast and General Surgery, Royal College of Surgeons, Glasgow, United Kingdom*
[3] *Dept. of Cell Pathology, Calderdale and Huddersfield NHS Foundation Trust, United Kingdom*
[4] *Dept. of Breast and Reconstructive Surgery, Calderdale and Huddersfield NHS Foundation Trust, United Kingdom*

Background/Purpose：The UK National Health Service Breast Screening Programme proposed five categories for reporting needle core biopsies of suspicious breast lumps. These range from B1 (normal tissue) to B5 (malignant). A B2 result is reserved for specimens that that contain a benign abnormality with little or no malignant potential. These commonly include fibroadenomas, fibrocystic change, duct ectasia and abscesses. This single centre study aimed to identify cases where an initial core biopsy was reported as B2 but the patient subsequently developed ipsilateral breast carcinoma. The initial B2 slides of these patients were then re-reviewed to identify potential histological markers that might herald the patient's subsequent diagnosis.

Methods：Spanning a 24 month period, all consecutive needle core biopsies of breast tissue were retrospectively identified and analysed using computer based histology reporting software. The initial reporting of the biopsy was noted and all subsequent biopsy results were also identified. Other data collected included the patient's age. From these results, all the patients that initially had a B2 biopsy who subsequently had a B5 biopsy or resection of breast carcinoma were identified. The histological slides of these patients were then re-reviewed by a consultant histopathologist with an interest in breast pathology.

Results：1465 sets of records were analysed in total. 162 had B1 diagnoses, 568 had B2 diagnoses, 65 had B3 diagnoses, 8 had B4 and 559 had B5 diagnoses. The remaining patients were given a diagnosis overlapping 2 categories (either 1/2 or 2/3). Of these, four patients who subsequently developed ipsilateral breast carcinoma (B5 result) had a B2 biopsy previously. The patients were all female, aged between 46-73 years at the time of the B2 diagnosis. The B2 diagnoses were fibrocystic change, fibroadenoma and benign microcalcification. Two of the patients subsequently developed ductal carcinoma in situ, while the other two developed invasive ductal carcinoma.

Conclusion：Four cases of B2 biopsies were identified that subsequently developed ipsilateral breast carcinoma. These were reviewed by a pathologist and radiologist to identify potential markers/patterns of microcalcification that may help predict the future incidence of carcinoma. This data will be presented at the conference.

PO01-11

EXERCISE IS ONE OF WAYS TO REDUCE THE RISK OF BREAST CANCER

Mita Septaria Hasugian, Jesslyn Luzalim

Dept. of Public Health, Univ. of Indonesia, Indonesia

Background/Purpose：This paper will explain the risk factors of breast cancer and how to prevent the risk factors of breast cancer. Breast cancer is the most common disease in developing countries, particularly in Indonesia. Breast cancer is the second most dangerous after cervical cancer. Breast cancer disease usually attacks women who aged over 40 years. However, young women only can be attacked breast cancer. Based on Health Profile Data 2007 showed that the proportion of breast cancer who were admitted to hospital in Indonesia increased for 3 consecutive years from 20.63% in 2004 to 22.8% in 2005 and to 26.74% in 2006 and was ranked first out of 10 types of cancer in the majority of hospitals in Indonesia, namely breast cancer. The case is greatly shocking condition to many people because it is increasing from year to year.

Methods：In regarding on making this paper, the authors using the methods of research literature.

Results：Obesity is one of the factors that causes the increase of breast cancer. This is evidenced by the data Riskesdas in 2007, the prevalence of overweight and obese population aged ≥ 15 years in Indonesia at 13.9% males and 23.8% in women. There is a very closed relation between the increase in breast cancer with excess weight, unbalanced diet and lack of activity.

Conclusion：In conclusion the risk management approach to the spread of breast cancer can be done by the way of diet and regular exercise. Setting a balanced diet through reducing the consumption of alcohol and fast food, regular exercise and increasing physical activity in daily activities as well will be one solution to reduce the risk factors of breast cancer.

PO01-12

MAMMARY GLAND DENSITY AND BREAST CANCER RISK: A CASE-CONTROL STUDY IN OKAYAMA AND KAGAWA REGIONS

Takayuki Motoki[1], **Naruto Taira**[1*], **Keiko Nishiyama**[1], **Taeko Mizoo**[1], **Yohichi Ishibe**[2], **Setsuko Ishihara**[3], **Takayuki Iwamoto**[1], **Tadahiko Shien**[1], **Junji Matsuoka**[1], **Hiroyoshi Doihara**[1]

[1] *Dept. of Breast and Endocrinological Surgery, Okayama Univ. Hospital, Japan*
[2] *Dept. of Surgery, Mizushima Kyodo Hospital, Japan*
[3] *Dept. of Radiology, Okayama Saiseikai General Hospital, Japan*

Background/Purpose : While giving birth is considered to reduce the risk of breast cancer, a high BMI is considered to reduce the risk before menopause and increase the risk after menopause. A high mammary gland density is also regarded as a risk-increasing factor, and the density decreases after giving a birth. By contrast, the BMI and mammary gland density are inversely correlated, showing a potential contradiction after menopause.

Methods : This was a case-control study performed in Okayama and Kagawa. The subjects were unilateral breast cancer patients (N=614) and examinees that had undergone screening were control subjects (N=1,542). The mammary gland density was judged independently by two examiners, based on the BI-RADS classification (category: C1-4), and inconsistent cases were finally judged by re-reading the images. The healthy side was examined in each patient, and the higher value was adopted in the control subjects with inconsistency between the bilateral breasts. Logistic regression analysis was performed regarding the number of births, BMI, and BI-RADS as factors, and the age-adjusted odds ratio and 95% confidence interval were calculated.

Results : The concordance rate of judgments was 98.4% (Cronbach α=0.99). The C1-4 rates (%) were 23, 42, 27, and 7 in the patients, respectively, and 26, 36, 32, and 7 in the control subjects, respectively. The mean BMI and number of births were 22.9 and 1.66 in the patients, respectively, and 22.7 and 2.1 in the control subjects, respectively. The number of births (unit odds ratio: 0.21 [95% confidence interval: 0.09-0.47]) was a significant factor before menopause, and the BMI (1.05 [1.01-1.09]) and number of births (0.57 [0.49-0.68]) were significant factors after menopause. Regarding the association with the mammary gland density, the odds ratios [95% confidence interval] of C2, 3, and 4 relative to C1 were 0.88 [0.53-1.5], 0.67 [0.4-1.11], 0.92 [0.48-1.78] (p for trend=0.287) before menopause, respectively, and 1.44 [1.04-1.99], 0.94 [0.62-1.42], and 2.13 [0.99-4.52] (p for trend=0.432) after menopause, respectively.

Conclusion : It was suggested that a high mammary gland density is a risk factor for breast cancer independent of giving birth and obesity in postmenopausal women.

PO02-01

DIETARY SUPPLEMENTS USE AFTER BREAST CANCER DIAGNOSIS AND QUALITY OF LIFE AMONG KOREAN BREAST CANCER SURVIVORS

Myungsook Park[1], **Eunkyung Hwang**[2],
Hyeong-Gon Moon[3], **Dong-Young Noh**[3], **Jung Eun Lee**[1*]

[1] *Dept. of Food and Nutrition, Sookmyung Women's Univ., Korea*
[2] *Breast Care Center, Seoul National Univ. Hospital, Korea*
[3] *Dept. of Surgery, Breast Care Center, Seoul National Univ. Hospital, Korea*

Background/Purpose : Breast cancer is the second most common cancer in Korean women. Although 5-year survival rate is high in Korea (91.0% in 2006-2010), there has been limited evidence about breast cancer survivor's dietary supplements use and health-related quality of life (HRQOL).

Methods : We examined dietary supplements use after breast cancer diagnosis in relation to HRQOL among a total of 162 Korean female breast cancer survivors in a cross-sectional study. Participants were asked to report their current use, duration and dose of dietary supplements after breast cancer diagnosis. HRQOL was measured by Korean-translated questionnaire of the European Organization for Research and Treatment of Cancer-C30 and BR23 modules. We used a general linear model to examine the association between dietary supplements use and HRQOL.

Results : 68.5% of survivors reported to currently use at least one product of nutrient supplements (e.g. multivitamin and vitamin C) or other types of dietary supplements (e.g. red ginseng and propolis). The three most commonly used nutrient supplements were multivitamin, vitamin C supplement and omega-3 fatty acids supplement; 37.7 % of survivors currently used multivitamin, 24.7 % used vitamin C supplement, and 22.2% used omega-3 fatty acids supplement. For other types of dietary supplements, red ginseng, propolis and mushroom were most commonly used; 23.5 % of survivors currently used red ginseng, 9.9% used propolis, and 6.8% used mushroom. Breast cancer survivors tended to consume multiple dietary supplements; 25.9% of survivors reported to currently use multivitamin with another nutrient supplements (e.g. omega-3 fatty acids and vitamin C) and 13.0% used multivitamin with other types of dietary supplements (e.g. red ginseng and propolis). When we examined the association between dietary supplements use and HRQOL, multivitamin user had low score of body image scale ($p=0.02$) and high score of fatigue scale ($p=0.04$) compared to non-user. Survivors who had low score of economic function scale tended to use more multivitamin ($p=0.02$), propolis ($p<0.001$) and other types of dietary supplements ($p=0.06$) compared to survivors with high score. Nutrient supplement users were more likely to have higher score of global health status scale compared to non-user ($p=0.04$). Breast cancer survivors who had high score of symptom scales tended to use other types of dietary supplements compared to those with low score ($p=0.03$ for nausea and $p=0.05$ for pain).

Conclusion : In our study, more than 60% of breast cancer survivors reported to currently use dietary supplements and its use may be related to quality of life.

PO02-02

THE ASSOCIATION OF AREA-LEVEL SOCIAL CLASS AND TOBACCO USE WITH ADVERSE BREAST CANCER CHARACTERISTICS AMONG WHITE AND BLACK WOMEN IN MARYLAND, 1992-2003

Ann C. Klassen[1*], **Aaron Pankiewicz**[1], **Stephanie Hsieh**[2], **Abigail Ward**[3], **Frank Curriero**[3]

[1] *Dept. of Community Health and Prevention, Drexel Univ. School of Public Health, U.S.A.*
[2] *Dept. of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, U.S.A.*
[3] *Dept. of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, U.S.A.*

Background/Purpose : For breast cancer, worse disease characteristics (aggressive histology, later stage, larger tumors) are associated with both fewer social resources and black race. However, there is incomplete understanding of whether social gradients have similar impact across race, and whether behavioral factors such as tobacco use contribute to social gradient effects.

Methods : 50062 breast cancer cases in white and black women diagnosed in Maryland from 1992-2003 were linked to block group indicators of tobacco use and social class. Multi-level models estimated the effect of area-level social class and tobacco consumption on tumor grade, size, and stage at diagnosis.

Results : Adjusting for race, age and year of diagnosis, higher social class was associated with lower risk for tumors diagnosed at SEER stage 2 or later (OR 0.90, 95% CI 0.88-0.92), histological grade 3 or 4 (OR 0.96, 95% CI 0.94-0.99) and tumor size >2 cm (OR 0.87, 95% CI 0.84-0.90), and higher tobacco spending was associated with higher risk (later stage OR 0.99, 95% CI 0.98-1.01; higher grade OR 1.01, CI 1.00-1.03; larger tumor OR 1.03, 95% CI 1.01-1.06). Social class was less protective for black women, but tobacco effects were not race-specific.

Conclusion : Results suggest differential protection of social class for black and white women, supporting use of intersectionality theory in breast cancer disparities investigations. Area-level tobacco consumption may capture cases' direct use and second hand smoke exposure, but also may identify neighborhoods with excess cancer-related behavioral or environmental exposures, beyond those measured by social class.

PO02-03

EPIDEMIOLOGY OF BREAST CANCER IN KYZYLORDA OBLAST OF KAZAKHSTAN

Ulpan Toleutay

Dept. of Public Health, Kazakhstan School of Public Health, Kazakhstan

Background/Purpose：Breast cancer in Kazakhstan and its Kyzylorda oblast is the most prevalent cancer in women and has increasing trends of incidence. The aim of study: to determine some features of epidemiology of breast cancer among women in Kyzylorda oblast of Kazakhstan.

Methods：A retrospective study was conducted for 21 years (1991-2011). Crude rates were calculated and methods of descriptive statistics were used. Statistical significance of differences was assessed using the criteria of paired T-test and Wilcoxon signed rank test with values of statistical error probability (p).

Results：The studied oblast is characterized by high rates of growth and differences in levels, as well as reduction of growth rates in some districts due to implementation of State programs aimed at improving of social and environmental condition in deprived areas. Rate of growth was most pronounced in the age group of 50-59 years old, while the highest incidence was at 60-69 years old. The high incidence was observed in Karmakshy district of Kyzylorda oblast. This may be due to environmental factors, and requires further investigation.

Conclusion：The findings will help in making administrative decisions to optimize organization of cancer care for breast cancer patients, as well as planning and implementation of activities aimed at prevention of breast cancer by improving environmental situation in oblast and social support for rural population.

PO03-01

BREAST CANCER SUSCEPTIBILITY ASSOCIATED SNP AND PROGNOSIS

Jun Woo Lee[1], **Wonshik Han**[2, 3], **Hyeong-Gon Moon**[2, 3], **Jisun Kim**[1], **Min Kyoon Kim**[2, 3], **Tae-Kyoung Yoo**[2, 3], **Jongjin Kim**[2, 3], **Eunshin Lee**[2, 3], **Dong-Young Noh**[2*]

[1] *Dept. of General Surgery, Seoul National Univ. Hospital, Korea*
[2] *Dept. of Surgery, College of Medicine, Seoul National Univ., Korea*
[3] *Cancer Research Institute, College of Medicine, Seoul National Univ., Korea*

Background/Purpose : After completion of human genome project, some genetic variants are discovered and highlighted by genome-wide association studies (GWAS). Single nucleotide polymorphism (SNP) are considered to be the key variations leading to the various breast cancer susceptibility between each individuals. In 2011, our group has validated 5 SNPs as significant risk factor of breast cancer in Korean women for the first time. Recently, there has been some attempts to find clinical meaning of SNPs in each breast cancer patient. But it was not successful.

Methods : Consecutive patients with histologically confirmed primary breast cancer subjected to operative procedures between 2002 and 2009 in Seoul National University Hospital were included for analysis. Patients diagnosed with noninvasive breast cancer (ductal carcinoma *in situ* and lobular carcinoma *in situ*) or stage IV breast cancer were excluded. Peripheral venous blood samples were obtained and stored at the time of operation. The SNPs genotyped included rs2046210 (6q25.1), rs2981582 (FGFR2), rs889312 (MAP3K1), rs3803662 (TOX3/TNRC9), and rs4973768 (SLC4A7). SNP genotyping was carried out on an Applied Biosystems 7900HT realtime PCR system (Applied Biosystems). We made collaboration with the Korean Central Cancer Registry (KCCR) to improve the validity of the mortality data. Total of 3,209 patients were included for survival and recurrence analysis.

Results : 492 (15.33%) patients had recurrence. And there were 277 (8.63%) mortalities overall. The median follow-up was for 85.59 month (±29.979). The GG genotype of SNP rs3803662 showed better survival than other AA, AG genotypes (cumulative survival was 89% vs. 84% at 120 months follow-up). And it is validated at multivariate analysis (p=0.024).

Conclusion : This study showed strong association between a certain genotype of single SNP and survival of breast cancer patients for the first time. Further lab investigation including functional study or studies on other races should be performed to find a novel or alternative hidden pathways of cancer progression.

PO03-01

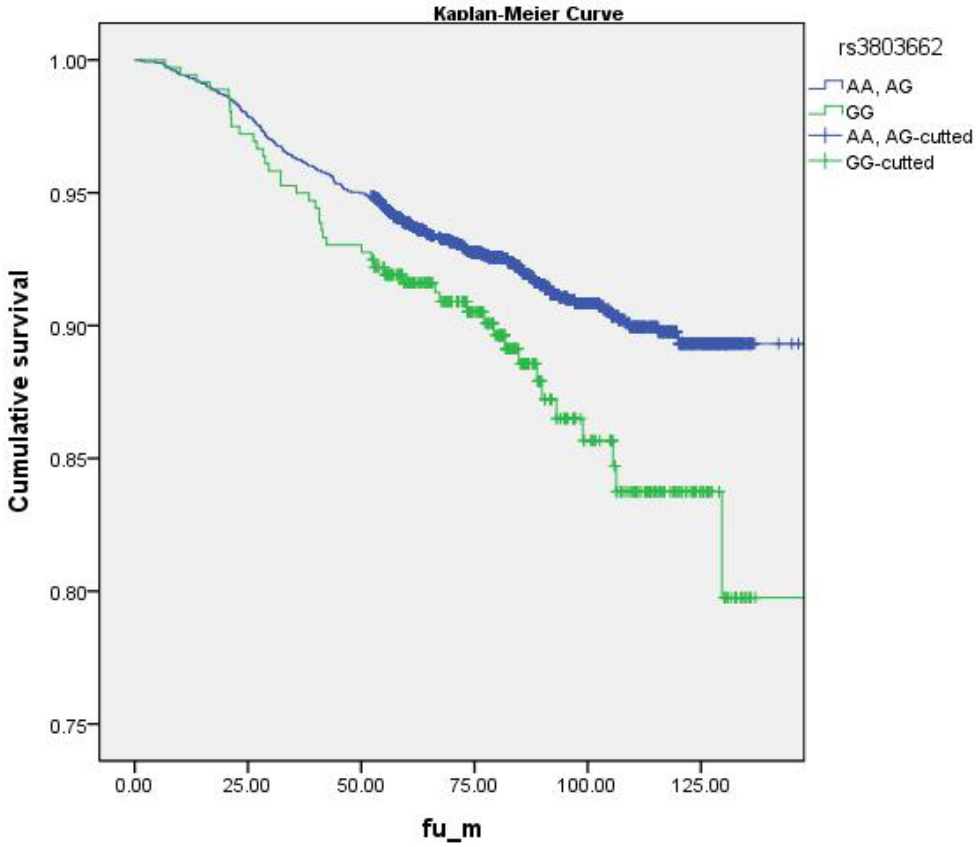

Figure 1

PO03-03

A STUDY PROJECT ON THE ROLE OF ACRIFLAVINE TO INHIBIT TUMOR INVASION AND MIGRATION IN HUMAN BREAST CANCER CELLS

Pei-Yu Chao[1*], **Tzu-En Lin**[1], **Yung-Wei Chiu**[2], **Jer-Yuh Liu**[3*]

[1] *Graduate Institute of Basic Medical Science, China Medical Univ., Taiwan*
[2] *Dept. of Emergency, Tungs' Taichung MetroHarbor Hospital, Taiwan*
[3] *Graduate Institute of Cancer Biology, China Medical Univ., Taiwan*

Background/Purpose : Resistance to chemotherapy and invasion/metastasis are the major problems facing breast cancer patients. Cisplatin is a chemotherapeutic agent not used routinely for breast cancer treatment because of acquired drug-resistance phenotype. Recent pharmacological screens have identified acriflavine as a drug that possesses potent inhibitory effects on mechanisms involving invasion and metastasis in several cancer cell types. The aim of this study was to compare in human breast cancer cells that acriflavine would have improved efficacy with decreased systemic toxicity over cisplatin on invasive/metastatic property. Underlying molecular events and mechanisms will be also discussed.

Methods : Four breast cancer cell lines, MDA-MB-231, MCF-7, Hs578T and MDA-MB-486, were tested. The cell viability (MTT) assay was employed as a primary screening method to determine the in vitro cytotoxicity and compare the effects of both agents, cisplatin and acriflavine. Molecular mechanisms underlying drug toxicity were probed using immunostaining, flow cytometry and immunoblotting. Target gene knockdown phenotypes were generated by shRNA techniques.

Results : Both cisplatin (10-50 μM) and acriflavine (1-5μM) induced apoptosis in a dose-dependent manner on all of four cell lines. The cell proliferation rate after subculture showed significant inhibition only in Hs578T cells. Both Hs578T and MDA-MB-486 cells were sensitive to cisplatin but drug-resistance showed in MDA-MB-231 and MCF-7 cells. The effect of acriflavine was much more potent in MDA-MB-231 and MCF-7 cells, even in low dose. PKC-knockdown breast cancer cells showed diverse resistance to both agents.

Conclusion : This preliminary report showed acriflavine a promising chemotherapeutic agent, especially in advanced breast cancer. The specific objectives of our entire project will be to: (1) compare the effects of diverse doses of cisplatin and acriflavine in cell viability, proliferation and apoptosis in four breast cancer cells lines; (2) determine the involvement of pro/anti-apoptotic proteins in cisplatin and acriflavine cytotoxicity; (3) determine the role of PKC downstream pathway on drug resistance; (4) examine the effects of PKC-knockdown breast cancer cells to chemotherapy responsiveness.

PO03-04

A RESVERATROL ANALOGUE RHAPONTIGENIN REGULATES ER STRESS RESPONSE IN MCF-7 CELLS

Jinsun Lee, Haekeung Kim, Jaeryong Kim, Eilsung Chang*

Dept. of General Surgery, School of Medicine, Chungnam National Univ., Korea

Background/Purpose : Disruption of physiological functions by ER stress response has been implicated in a wide range of human diseases including breast cancer. Investigations into the molecular mechanism underlying severe ER-stress could provide important information that would increase our understanding of cancer progression and provide specific targets for therapeutic intervention.

Methods : Rhapontigenin was isolated from rhizome of rhubarb. RT-PCR was used for measuring mRNA levels of glucose-regulated protein78 and GADD153, and XBP-1 splicing. Protein levels of these proteins were measured by western blot analysis. Apoptosis was observed by western blotting using various antibodies and flow cytometric analysis. Cell viability was determined by CCK8 assay.

Results : Rhapontigenin induces the inositol-requiring enzyme1α, following cytoplasmic splicing of X-box binding protein-1 was elevated by treatment of MCF-7 cells with 10 μM rhapontigenin for 72 h. mRNA and protein levels of glucose-regulated protein78 were up-regulated by rhapontigenin. GADD153 was robustly expressed at mRNA and protein levels by rhapontigenin. ER-specific caspases such as caspase-12, caspase-4, and caspase-9 were activated by rhapontigenin. Following caspase-3 and PARP cleavage, the activity of caspase-3 was stimulated by rhapontigenin, and the activation of caspase-3 was restricted by the general caspase inhibitor z-VAD-fmk. Apoptotic cells were sorted by flow cytometry and identified using propidium iodide staining, revealing a marked accumulation of sub-G1 DNA content. Rhapontigenin-induced inhibition of cancer cell growth was dose-dependent after 72 h of treatment, showing a significant reduction at rhapontigenin concentrations over 5 μM.

Conclusion : The mechanisms therefore contain potential candidates for novel targets in development of anti-cancer drugs.

PO03-06

S6K1 INHIBITION ENHANCES TAMOXIFEN-INDUCED CELL DEATH IN MCF-7 CELLS THROUGH

Jangmoo Byeon[1], **Eun-Kyu Kim**[1], **In-Chul Park**[2], **Hyun-Ah Kim**[1], **Min-Ki Seong**[1], **Joo-Young Lee**[1], **Yeon-Joo Son**[1], **Woo Chul Noh**[1*]

[1] *Dept. of Surgery, Korea Cancer Center Hospital, Korea*
[2] *Division of Radiation Cancer Research, Korea Institute of Radiological & Medical Sciences, Korea*

Background/Purpose : S6 kinase 1 (S6K1) was suggested to be a marker for endocrine therapy resistance in breast cancer. We examined whether tamoxifen's effect can be modulated by S6K1 inhibition.

Methods : Cell viability was determined by MTT assay. The synergistic effects of 2-drugs were assessed by isobologram analysis. S6K1, Mcl-1 or survivin siRNAs were transfected to investigate the role of S6K1, Mcl-1, and survivin in tamoxifen-induced cell death.

Results : S6K1 inhibition by PF4708671, a selective inhibitor of S6K1, acts synergistically with tamoxifen in S6K1-high MCF-7 cells. Similarly, the knockdown of S6K1 with siRNA significantly sensitized MCF-7 cells to tamoxifen. Inhibition of S6K1 by PF4708671 led to a marked decrease in the expression levels of the anti-apoptotic proteins Mcl-1 and survivin, which was not related to mRNA levels. In addition, suppression of Mcl-1 or survivin, using specific siRNA, further enhanced cell sensitivity to tamoxifen.

Conclusion : These results showed that inhibition of S6K1 acts synergistically with tamoxifen, via translational modulation of Mcl-1 and survivin. Based on these findings, we propose that targeting S6K1 may be an effective strategy to overcome tamoxifen resistance in breast cancer.

PO03-07

PROGNOSTIC VALUE OF MUTANT TP53 IN BASAL BREAST CANCER

Jung Eun Choi[1], **Jeong Yeong Park**[1], **Ji Hoon Lee**[1], **Gi Tak Son**[1], **Su Hwan Kang**[1], **Young Kyung Bae**[2], **Soo Jung Lee**[1*]

[1] *Dept. of Surgery, College of Medicine, Yeungnam Univ., Korea*
[2] *Dept. of Pathology, College of Medicine, Yeungnam Univ., Korea*

Background/Purpose : p53 is a tumor suppressor gene that plays an important role in cell cycle control and apoptosis. In the breast cancer, mutant tumor protein (TP53) is expressed in approximately 30% and patients with mutant TP53 often tend to have poor response to chemotherapy and poor prognosis than those with normal TP53. But, according to a recent study, TP53 inactivation could cause to significant DNA damage and to eventual cell death by mitotic catastrophe. We investigated the expression frequency and prognostic value of mutant TP53 using tissue microarrays of 898 invasive breast cancers.

Methods : From January 1995 to December 2005 at Yeungnam university hospital, patients who diagnosed with the primary invasive breast cancer and received operation were included in this study. Patients with bilateral breast cancer or distant metastasis at the time of diagnosis were excluded. According to the immunohistochemical results of estrogen receptor, progesterone receptor, human epidermal growth factor 2, Ki-67, epidermal growth factor and cytokeratin 5/6, we classified patients into 6 subgroups, luminal A, luminal B1, B2, HER2-enriched, normal breast-like (triple negative non-basal) and basal-like breast cancers. Immunohistochemical staining for TP53 was performed and we defined more than 10% stain of tumor cell as mutant TP53-positive. Distribution and prognostic significance of mutant TP53 in each subgroup was investigated.

Results : In 898 invasive breast cancers, mutant TP53 was identified in 33.5% (301/898). Each expression frequency of mutant TP53 was 10.9% (42/385) in luminal A, 32.1% (45/140) in luminal B1, 50.0% (34/68) in luminal B2, 63.7% (72/113) in HER2-enriched, 54.7% (35/64) in normal breast-like and 57.0% (73/128) in basal-like subtype, respectively. In whole breast cancer patients, patients with mutant TP53 tended to have poor overall survival (OS) and disease free survival (DFS). However, there was no statistical significance ($p=0.187$ and $p=0.651$, respectively). But, in 128 patients with basal-like breast cancer, mutant TP53 showed good prognosis in both OS and DFS ($p=0.003$ and $p=0.021$, respectively). In basal-like breast cancer, the expression of mutant TP53 had no association with other clinicopathologic factors such as tumor size, lymph node metastasis, histological grade, lymphovascular invasion etc. and 98.4% (126/128) patients received adjuvant chemotherapy. In multivariate analysis, expression of mutant TP53 was an independent prognostic factor for OS and DFS in basal-like breast cancers ($p=0.008$ and $p=0.012$, respectively).

Conclusion : This study showed that basal-like breast cancer with mutant TP53 has a good outcome in both OS and DFS. Further studies are needed to identify the action mechanism of mutant TP53.

PO03-08

TUMOR VOLUME AND PROPORTIONAL SIZE MEASUREMENT ARE LESS EFFICIENT IN PREDICTING NODE METASTASIS WHEN COMPARED TO THE CONVENTIONAL TUMOR SIZE MEASUREMENT

Jongjin Kim[1], **Wonshik Han**[1], **Hyeong-Gon Moon**[1], **Jisun Kim**[1], **Jun Woo Lee**[1], **Min Kyoon Kim**[1], **Tae-Kyung Yoo**[1], **Eunshin Lee**[1], **Woo Jyung Moon**[2], **Nariya Cho**[2], **Jung Min Chang**[2], **Dong-Young Noh**[1,3*]

[1] *Dept. of Surgery, College of Medicine, Seoul National Univ., Korea*
[2] *Dept. of Radiology, College of Medicine, Seoul National Univ., Korea*
[3] *Cancer Research Institute, College of Medicine, Seoul National Univ., Korea*

Background/Purpose : Although the present TNM staging system uses the largest tumor diameter (Tmax) for T-staging, the optimal method of T-staging is controversial. Several recent studies suggested that the tumor volume and proportional size of the tumor can be more accurate for staging or predicting axillary lymph node metastasis (ALNM). The purpose of this study is to compare the conventional Tmax and other novel tumor measurement methods in predicting ALNM in patient with invasive breast cancer.

Methods : This study included 418 patients who underwent surgery due to invasive breast cancer in the Seoul National University Hospital Breast Care Center. Tumor volume (TV) was calculated based on the three-dimensional diameters of tumor obtained from the pathology report. To calculate proportional tumor size, we used VolparaTM breast volumetry to determine the breast volume (BV) and glandular volume (GV).

Results : The ROC curves for ALNM prediction showed that Tmax, TV, TV/BV ratio and TV/GV ratio all had significant correlation with the presence of ALNM. However, there was no statistically significant difference between the novel tumor measurement methods and the conventional tumor size measurement. The AUCs for each method were 0.698, 0.693, 0.694, and 0.686 for Tmax, TV, TV/BV, and TV/GV, respectively. When adjusted for other clinicopathologic factors, Tmax showed the highest odd ratio for having ALNM (OR=1.456, 95% CI=1.143-1.854) when compared to other novel tumor measurement methods (OR=1.039 for TV, OR=1.029 for TV/BV, OR=1.005 for TV/GV).

Conclusion : Conventional T staging, which measures the largest diameter of the tumor (Tmax), is the most reliable predictor of ALNM when compared to other recently proposed tumor measurement methods.

PO03-09

A PEPTIDE-GUIDED HYDROPHOBICALLY MODIFIED GLYCOL CHITOSAN NANOPARTICLES IS VERY USEFUL FOR TARGETING TRIPLE NEGATIVE BREAST CANCER

Ho Yong Park[1], **Hyang Hee Choi**[1], **Jin Gu Kang**[1], **Seung Ook Hwang**[1], **Wan Wook Kim**[1], **Jin Hyang Jung**[1], **Jong-Ho Kim**[2], **Sang Mun Bae**[2], **Byung-Heon Lee**[2], **In-San Kim**[2*]

[1] *Dept. of Surgery, School of Medicine, Kyungpook National Univ., Korea*
[2] *Dept. of Biochemistry and Cell Biology, School of Medicine, Kyungpook National Univ., Korea*

Background/Purpose : MDA-MB-231 is cell line of triple-breast cancer with interleukin-4 receptor (IL-4R) positive. The purpose of this study was to demonstrate nanoparticles facilitates cellular uptake and chemotherapeutic efficacy of nanoparticles conjugated with IL-4R binding peptide (I4R) loaded with paclitaxel (PTX) in MDA-MB-231.

Methods : We developed hydrophobically modified glycol chitosan (HGC) nanoparticles conjugated with I4R (HGC-I4R) and PTX-loaded HGC-I4R. Tumor-bearing mice were injected once every 3 days for 15days with saline, free PTX, PTX-HGC or PTX-HGC-I4R solutions. Imaging study was performed by labeling nanoparticles with the near-infrared fluorophore.

Results : The cell binding and uptake of HGC-I4R nanoparticles were more increased than HGC in MDA-MB-231. Tumor volume and weight were significantly decreased in PTX-loaded HGC-I4R treatment compared with the control of PTX-HGC ($p=0.0142$). Cancer image 24 hours after intravenous injection showed strong signals in the HGC-I4R compared to weaker signals in the corresponding HGC. HGC-I4R nanoparticles showed a later, higher peak accumulation and slow clearance than HGC.

Conclusion : Our study demonstrated novel peptide-guided nanoparticles that facilitated intracellular uptake, resulting in effective targeted-tumor therapy in breast tumor tissue and MDA-MB-231.

PO03-10

THE RELATIONSHIP BETWEEN ER/PR RECEPTOR AND EXPRESSION OF MTOR/PAKT PROTEINS

Sun Wook Han[1], **Zi Sun Kim**[2], **Chul Wan Lim**[2], **Min Hyuk Lee**[3], **Sung Yong Kim**[1*]

[1] *Dept. of Surgery, Soonchunhyang Univ., Cheonan Hospital, Korea*
[2] *Dept. of Surgery, Soonchunhyang Univ., Bucheon Hospital, Korea*
[3] *Dept. of Surgery, Soonchunhyang Univ., Seoul Hospital, Korea*

Background/Purpose : The phosphatidylinositol 3-kinase(PI3K)/Akt/mammalian target of rapamycin (mTOR) pathway is a critical signaling pathway downstream of the growth factor receptor tyrosine kinase that regulates cell growth and survival. Rapamycin, an inhibitor of the mTOR, possesses antitumor activity against many tumor including breast cancer, especially against ER positive breast cancer cell lines. In this study, the expression of mTOR and pAkt in breast cancer, its association with ER/PR receptors and prognosis were examined.

Methods : Formalin fixed paraffin-embedded 170 cases of the breast cancer were immunohistochemically stained, using rabbit monoclonal antibody mTOR (1:100, clone 49F9, Cell Signalomg Technology, Danvers, MA, USA) and rabbit monoclonal antibody pAkt (1:50, clone 736E11, Cell Signaling Technology, Danvers, MA, USA).

Results : mTOR expression was positive in 110 of 170 cases (64.7%) and pAkt expression was positive in 130 of 170 cases (76.5%). In correlation between clinicopathologic factors and mTOR/pAkt expression, mTOR expression was correlated with ER/PR positive and pAkt expression was correlated with age (> 65 years), postmenopause. But there is no statistically significant in correlation between survival and mTOR/pAkt expression.

Conclusion : The results provide a rational basis for future clinical development of mTOR inhibitor combined ER inhibitor in breast cancer.

PO03-11

THE ASSOCIATION BETWEEN STEM CELL AND MOLECULAR SUBTYPES

Yoon Seok Kim, Dong Won Ryu, Chung Han Lee*

Dept. of General Surgery, Kosin Univ. Gospel Hospital, Korea

Background/Purpose : Breast cancer is highly heterogeneous disease, which displays varying molecular and clinical features, and therapeutic resistance is a frequently encountered problem. Despite increased knowledge, many patients will develop metastatic disease. One theory that could explain treatment failure is cancer stem cell theory. Cancer stem cells defined as a subset of tumor cells with stem cell-like features have the capacity to self-renew and differentiate, giving rise to a heterogeneous tumor cell population. In this study, we investigated the association between the proportion of CD44+/CD24-/low cells, ALDH1+ cells, CD44+/CD24-/low/ALDH1+ cells in primary breast cancer tissue and breast cancer subtypes.

Methods : We investigated the association between the proportion of CD44+/CD24-/low cells, ALDH1+ cells, CD44+/CD24-/low/ALDH1+ cells in primary breast cancer tissue and breast cancer subtypes who underwent breast cancer operation in Kosin University Gospel Hospital from July 2005 to March 2008. A total of 198 patients were included. To identify the CD44+,CD24-/low, ALDH1+ cells in routine surgical specimens, the cancer cases were analysed by immunohistochemistry staining, and the results were analysed to correlate the amount and distribution of the CD44+,CD24-/low, ALDH1+ population with breast cancer subtypes.

Results : Basal-like tumors contained the higher percentage of cells with cancer stem cell phenotype, CD44+/CD24-/low and ALDH1+ cells. The analysis of breast cancer cell lines indicated that luminal subtype are enriched in a CD44-/low/CD24+ cell population.

Conclusion : The proportion of CD44, CD24 and ALDH1 phenotypes seem to associated with molecular subtypes. It seems that the identification of cancer stem cell within the distinct molecular subtypes is important, because it is pivotal to translate the cancer stem cell concept to clinical practice. To identify cancer stem cell within the molecular subtypes, more study will be needed.

PO03-12

MEDULLARY CARCINOMA OF THE BREAST IN COMPARISION WITH INVASIVE DUCTAL CARCINOMA WITH MEDULLARY-LIKE FEATURES : CLINICOPATHOLOGIC CHARACTERISTICS AND PROGNOSIS

Kwang Kuk Park, Chung-Han Lee*, Dong-Won Ryu

Dept. of Surgery, College of Medicine, Kosin Univ., Korea

Background/Purpose : Medullary carcinoma of the breast is a variant of breast cancer characterized by the histologic appearance of poorly differentiated cells surrounded by a prominent lymphoid stroma. Patients with this pattern of breast carcinoma are considered to have a better prognosis than those with other histological subtypes. The purpose of this study is to compare the clinical characteristics and long term outcome of medullary carcinoma to invasive ductal carcinoma with medullary-like feature.

Methods : We conducted a retrospective analysis of 26 patients diagnosed medullary carcinoma of the breast and 25 patients with invasive ductal carcinoma with medullary-like feature from January 2001 to December 2008 of at Kosin University Gospel Hospital. The clinicopathologic features, disease free survival and overall survival for patients with medullary carcinoma were compared with those of the invasive ductal carcinoma with medullary-like feature patients.

Results : Early stage cancer was more frequent at medullary carcinoma and lymph node positive cancer was less frequent at medullary carcinoma. The expression of estrogen receptor was positive in either the TMC (5.6%) as compared to the and invasive ductal carcinoma with medullary-like feature (26.1%), and the difference was significant ($p<0.001$). The HER-2/*neu* expression rate was significantly lower in the medullary carcinoma (5.6%) than in the and invasive ductal carcinoma with medullary-like feature (21.7%, $p<0.002$). All patients in both groups are alive. Recurrence occurred in 2 patients of medullary breast cancer group (8%) and 2 patients of and invasive ductal carcinoma with medullary-like feature group (8%). All recurrence were occurred on contralateral breast.

Conclusion : Medullary breast cancer and invasive ductal carcinoma with medullary-like feature have a similarly favorable prognosis.

PO03-13

SYNERGIC LONG-TERM EFFECT OF COMBINATION WITH EXPANDED NK CELL AND IRRADIATION AGAINST HUMAN BREAST CANCER CELLS

Min-Ho Park[1*], **Youn-Seung Jung**[2], **Min-Jung Hwang**[1], **Young-Jae Ryu**[1], **Sun-Hyoung Shin**[1], **Duck Cho**[3], **Jung-Han Yoon**[1]

[1] *Dept. of Surgery, Chonnam National Univ. Hwasun Hospital, Korea*
[2] *Dept. of Surgery, Gwangju Hyundai Hospital, Korea*
[3] *Dept. of Laboratory Medicine, Chonnam National Univ. Hwasun Hospital, Korea*

Background/Purpose : Combination of NK-cell therapy and irradiation was reported to be a promising strategy for cancer. However, it is hard to reveal the synergic effect on the combination by the single-point cytotoxicity assay (i.e., 4 h). To find an *in vitro* experimental evidence on the synergic effect on combination of expanded NK cells and irradiation, clonogenic cell survival assay was applied.

Methods : Expansion of NK cells of peripheral blood mononuclear cell from healthy donors was done with irradiated K562-mb15-41BBL and 10-100 IU/mL human IL-2 and IL-15 (10 U/mL). The NK-sensitive Ewing sarcoma cell line ES8, breast cancer cell lines MDA-MB-231 and SKBR3 were irradiated with Cesium-137 gamma-ray at various irradiation dose. The experiments were performed at different condition: 1) control (no NK, no RT) group, 2) NK alone group, 3) RT alone group, and 4) NK+RT group. Single-point cytotoxicity assay (4 hr) was measured at 1:1 effector-to-target (E:T) ratio by a flow cytometry-based method using Calcein-AM and clonogenic cell survival assay (2 weeks) was also used.

Results : The cytotoxicity of expanded NK cells (n=3) against non-irradiated ES8, MDA-MB-231, and SKBR3 cells at 1:1 E:T ratio was 61.2%, 20.5% , and 36.6%, respectively. In single-point cytotoxicity, no significant difference between 4 groups was observed. The survival of ES8, MDA-MB-231 and SKBR3 cells in control group was 100.0%-100.0%-100.0%, in NK alone group was 7.5%-16.0%-81.1%, in RT alone group was 21.5%-13.9%-22.9% (2Gy), 5.3%-4.1%-11.1% (4Gy), and 0.5%-0.7%-2.3% (6Gy), and in NK+RT group was 0.8%-5.3%-13.9% (2Gy), 0.0%-4.1%-3.7% (4Gy), and 0.0%-0.4%-2.3% (6Gy). In long term clonogenic assay, the cell survival significantly decreased in combination group as compared to NK cell or radiation alone.

Conclusion : Based on our clonogenic cell survival assay, we can suggest that combination treatment with radiation and expanded NK cells had a synergistic effect on breast cancer cells.

PO03-14

A REPORT OF SECRETORY BREAST CARCINOMA WITH VARIOUS CHARACTER AND TREATMENT

Seung Pil Jung[1], **Hye Yoon Lee**[1], **Sinill Kim**[1], **Hoon Yub Kim**[1], **Insun Kim**[2], **Jeoung Won Bae**[1*]

[1] *Division of Breast and Endocrine Surgery, Dept. of Surgery, College of Medicine, Korea Univ. Hospital, Korea*

[2] *Dept. of Pathology, College of Medicine, Korea Univ. Hospital, Korea*

Background/Purpose : Secretory breast carcinoma is very rare and distinct subtype of breast cancer, characterized by the presence of intracellular and extracellular secretory material. The tumor has favorable clinical course and systemic involvement is extremely rare. Because most studies of this tumor have been case reports or separate analysis, the characteristics and optimal treatment strategies have not been fully elucidated due to its rarity.

Methods : To add further evaluation on this disease, we report 3 cases of this disease in which we described various patient with different age, hormone receptor status and treatment methods.

Results : An 84-year-old female patient complained with 1.2cm sized nodular density mass in lower inner quadrant of right breast. We performed a lumpectomy and sentinel lymph node biopsy. The tumor was not stained for estrogen receptor, progesterone receptor and c-erbB-2. Immunohistochemical stain revealed that the tumor was positive for distase resistant, periodic acid-Shiff (D-PAS and PAS) and Alcian blue. The tumor was finally diagnosed as secretory breast carcinoma. Two sentinel lymph nodes were harvested and were not involved by cancer cells. She did not receive adjuvant chemotherapy and after 61 months follow up period, there was no evidence of recurrence of breast carcinoma. A 62-year-old female patient complained of bloody discharge from right nipple. After breast sonserving surgery, the tumor was strongly stained for estrogen receptor (Allred score 8) and progesterone receptor (Allred score 6). And c-erbB2 was negative. PAS stain was positive and the tumor was diagnosed as secretory breast carcinoma. There was no evidence of cancer invasion in three sentinel lymph nodes. She underwent adjuvant radiation therapy and hormonal therapy with an aromatase inhibitor. During 21 months after opretaion, there was no evidence of disease recurrence. A 23-year-old female patient was underwent breast conserving surgery due to 0.8cm sized secretory breast carcinoma. The carcinoma was stained estrogen receptor as Allred score 4. Whereas the tumor stained negative for progesterone receptor (Allred score 0) and c-erbB-2. The sentinel lymph nodes were negative for cancer metastasis in two harvested nodes. The patient underwent radiation therapy and doxorubicin and cyclophosphamide based chemotherapy. During a 14 months follow-up period no relapse was observed.

Conclusion : Secretory breast carcinoma is very rare disease and there is no consensus about the treatment. As in our cases, the tumor could occur at various ages. The symptoms and clinical characteristics also may differ from each patient. Therefore, therapeutic option could be decided by the patients overall status and the characteristics of this rare disease.

PO03-15

SODIUM TANSHINONE IIA SULFONATE ATTENUATES EPIRUBICIN-INDUCED APOPTOSIS IN MCF-7 BREAST CANCER CELLS

Chun-Hsiang Cheng[1], **Ya-Chi Chan**[2], **Shou-Jen Kuo**[3], **Yu-Fen Wang**[4], **Dar-Ren Chen**[5*]

[1] *Medical Education and Research, Cancer Research Center, Changhua Christian Hospital, Taiwan*
[2] *Cancer Research Center, Changhua Christian Hospital, Changhua, Taiwan*
[3] *Dept. of Surgery, Changhua Christian Hospital, Taiwan*
[4] *Dept. of Pathology, Cancer Research Center, Changhua Christian Hospital, Taiwan*
[5] *Dept. of Surgery, Cancer Research Center, Changhua Christian Hospital, Taiwan*

Background/Purpose：Epirubicin was the most frequently used agents for treating breast cancers. The only drawback is it may result in cardiomyopathy. Sodium tanshinone IIA sulfonate (STS), a water-soluble derivative of tanshinone IIA, has been widely used as a Chinese medicine for cardiovascular protection. Our previous study showed that STS might protect rat cardiomyocytes from epirubicin-induced cytotoxicity. However, in human breast cancer cell lines BT-20 and MCF-7, the anti-cancer activity of epirubicin may be declined when combined with high concentration of STS. This study was aimed to investigate the action mechanisms of STS on epirubicin-induced apoptosis in MCF-7.

Methods：After treated with STS and epirubicin, cells were harvested for analyses. Cytotoxicity was determined by using MTT assay and trypan blue exclusion assay. With flow cytometry, annexin-V/PI staining was used for distinguishing viable, apoptotic and necrotic cells. To explore involvement of possible signaling pathways, including PI3K/Akt, mitogen-activated protein kinase (MAPK) and mitochondria pathways, Western blotting and flow cytometry were also performed.

Results：STS decreased the epirubicin-induced cytotoxicity, especially apoptosis. Epirubicin treatment led to decreased the phosphorylation of PI3K, AKT and ERK, and increased Bax/Bcl-2 ratio. When combined with STS, the actions were reversed.

Conclusion：STS could attenuate epirubicin-induced cytotoxicity in breast cancer cells through PI3K/AKT and ERK pathways. The mitochondria pathway may be also involved. Therefore, to avoid interference with chemotherapy, patients with breast cancer should ask the doctor's opinion regarding to non-regular treatment during chemotherapy.

PO03-16

SODIUM TANSHINONE IIA SULFONATE PRETREATMENT PROTECTS RAT CARDIOMYOCYTES FROM EPIRUBICIN-INDUCED CARDIOTOXICITY

Ya-Chi Chan[1], **Dar-Ren Chen**[2*], **Hsun-Hsia Chien**[3], **Yu-Shu Cheng**[4]

[1] *Cancer Research Center, Changhua Christian Hospital, Taiwan*
[2] *Dept. of Surgery, Cancer Research Center, Changhua Christian Hospital, Taiwan*
[3] *Division of Cardiovascular Medicine, Changhua Christian Hospital, Taiwan*
[4] *Dept. of Surgery, Changhua Christian Hospital, Taiwan*

Background/Purpose : Sodium tanshinone IIA sulfonate (STS), a water-soluble derivative of tanshinone IIA, has been widely used as a Chinese medicine for cardiovascular protection. Epirubicin is an anthracycline drug usually used for chemotherapy; however, it always induces cardiotoxicity and may lead to cardiomyopathy and heart failure. This study was aimed to evaluate the protective effects of STS pretreatment before epirubicin exposure on rat cardiomyocyte and related cellular mechanism.

Methods : H9c2 cells were treated with STS pretreatment (0.3125, 20 μM) for 2 or 24h followed by 1.7 μM epirubicin for 24h, then cells were harvested for analyses. Cells with subsequent incubations with drug-free medium or STS-included medium were also examined. Compared to the treatment without STS pretreatment, the cell viability was significantly increased after 20-μM STS pretreatment with following epirubicin exposure. STS pretreatment relived epirubicin-induced apoptosis and the relevant changes, such as increased ROS levels, MMP loss, NFκB translocation to nucleus and intracellular Ca2+ overloading. It also protected intracellular troponin I protein from damages.

Results : Those in vitro findings indicated that STS pretreatment may prevent cardiomyocytes from epirubicin-induced apoptosis through ROS and calcium signaling pathways.

Conclusion : STS may have potential to ease epirubicin-induced cardiotoxicity. Further in vivo evaluations of efficacy of STS combined with epirubicin are needed.

PO03-17

AN ENDOGENOUS ARYL HYDROCARBON RECEPTOR LIGAND INHIBITS PROLIFERATION OF HUMAN BREAST CANCER

Zhengdong Li[1], **Xinwei Yang**[2], **Zhigang Zhuang**[1], **Kai Wang**[1], **Xiaowen Tong**[3*]

[1] *Dept. of Breast, School of Medicine, Tongji Univ., Shanghai First Maternity and Infant Hospital, China*
[2] *Dept. of Traditional Chinese Medicine Surgery, Shanghai TCM Hospital, China*
[3] *Dept. of Obstetrician/Gynecologist, School of Medicine, Tongji Univ., Tongji Hospital, China*

Background/Purpose : The aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor mediates many biological processes. It is reported that AhR is highly expressed in different types of cancer, including breast cancer. However the functional roles of AhR in the breat cancer development remain poorly understood. Herein, we investigated if 2-(1'H-indole-3'-carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE, an endogenous AhR ligand) regulated proliferation and migration of human breast cancer cells via AhR using both estrogen receptor-positive (T47D and MCF7) and -negative breast cancer cell lines (MDA-MB-231 and MDA-MB-468).

Methods : Tissue microarray was used to assess the immunohistochemical expression levels of AhR in breast lesions (carcinoma tissues, normal tissue) as well as the correlation between AhR expression and clinicopathologic parameters. RT-PCR and Western blot were performed to detect the activation of AhR in response to ITE treatment. Also cell proliferation and migration were investigated using crystal violet assay and transwell chamber assay, respectively.

Results : We found that AhR was widely present in many histotypes of breast cancer tissues, but not in the normal tissues. No difference was detected between the grades, stages, and TNM classifications for each histotype of breast cancer tissues studied. ITE time-dependently activated AhR in these four breast cancer cell lines. Meanwhile, ITE significantly suppressed cell proliferation in T47D, MCF7 and MDA-MB-468, but not MDA-MB-231 cells in vitro. However compared to ER+ breast cancer cells, ER- breast cancer cells are less susceptible.

Conclusion : These data suggest that AHR is a potential new target for treating patients with breast cancer. ITE may be potentially used for therapeutic intervention for at least ER-positive breast cancer.

PO03-18

PROGNOSTIC AND PREDICTIVE VALUE OF TUMOR-INFILTRATING LYMPHOCYTES IN TRIPLE NEGATIVE BREAST CANCER

Eunmee Park[1], Keehoon Hyun[1], Wooseok Byon[1], Yonglai Park[1], Sungim Do[2], Swan Chae[2], Chanheun Park[1*]

[1] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Kangbuk Samsung Medical Center, Korea*
[2] *Dept. of Pathology, School of Medicine, Sungkyunkwan Univ., Kangbuk Samsung Medical Center, Korea*

Background/Purpose : Previous preclinical and clinical data suggest that increased lymphocytic infiltration would be associated with good prognosis and benefit from immunogenic chemotherapy especially in triple negative breast cancer (TNBC). We investigated single-center experience of TNBC and relationship with lymphocytic infiltration.

Methods : From January 2004 to December 2012, at department of surgery, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, we retrospectively reviewed 897 breast cancer patients-clinical outcomes, clinicopathological characteristics, breast cancer subtypes. And we reviewed lymphocytic infiltration of TNBC specimens by two pathologists. Statistical analysis of risk factors associated with recurrence was performed.

Results : A total of 897 patients, 76 were TNBC (8.47%). Mean age of TNBC patients were 50.95 (SD 10.42) years, mean follow-up periods was 40.06 months. We reviewed 49 slides, and there were 8 recurrent breast cancer patients (16.32%), and 4 patients were expired (8.16%). There were 9 lymphocytic predominant breast cancers (LPBC) - carcinomas with either intratumoral lymphocytes in > 60% of tumor cell nests. Patient of LPBC was recurred and 8 were not. In multivariate logistic regression, the odds ratio of lymphocytic infiltration was 0.59 (p=0.643).

Conclusion : In a single-center experience of TNBC, the lymphocytic infiltration in tumor cell nest might be good trend on the prognosis but there was not statistically significant. Further study with more patients will be needed.

PO03-18

Table 1. clinicopathological characteristics

TNBC	**76(total 897 breast cancer patients 8.47%)**			
Age	50.95(±10.42)			
Follow-up	40.06(±22.31)months			
Stage	DCIS 1		I 29	
	II 39		III 6	
	IV 1			
Reviewed TNBC slides	49 patients			
T-stage	T1	16	T2	29
	T3	3	T4	1
N-stage	N0	22	N1	14
	N2	7	N3	6

Table 1

Table 2. LPBC patients

	Recurred patients	Non-recurred patient	
LPBC	1	8	9
Non-LPBC	33	7	40

Table 2

Table 3. multivariate analysis

	Odd ratio	P value
LPBC	0.59	0.643
Age	0.96	0.415
N stage	1.72	0.111
size	2.79	0.063

Table 3

PO04-01

THE RELATIONSHIP BETWEEN PROGNOSIS AND PATHOLOGICAL COMPLETE RESPONSE IN BREAST CANCER PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY

Hidemi Kawajiri*, Tsutomu Takashima, Shinichiro Kashiwagi, Satoru Noda, Naoyoshi Onoda, Tetsurou Ishikawa, Kosei Hirakawa

Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan

Background/Purpose : The prognostic significance of pathological complete response (pCR) on intrinsic subtypes of breast cancer is controversial. The aim of the present retrospective study was to ascertain the significance of pCR on overall survival (OS) and disease-free survival (DFS) in each disease subtype.

Methods : A review of our institutional database identified 90 patients with operable breast cancer (stages IIA to IIIA) who received the same neoadjuvant chemotherapy (NAC) regimen.

Results : Of these 90 patients, pCR was observed in 38 (42%). Univariate analysis showed that T1 tumors (p=0.013), estrogen receptor-negative tumors (p=0.028), and progesterone receptor-negative tumors (p=0.029) were significantly associated with a high pCR rate. At the median follow-up time of 53months, 10 of 90 (11.1%) patients were dead and 20 of 90 (22.2%) patients were dead or had recurrences. Three of the 48 (6.3%) patients with the luminal subtype, six of the 27 (22.2%) patients with the triple negative (TN) subtype, and one of the 15 (6.7%) patients with theHER2-positivesubtype were dead. The OS of patients with TN tumors was significantly shorter than that of patients with other disease subtypes (p=0.016). The DFS of patients with luminal tumors was longer than that of patients with other disease subtypes. Survival was improved with pCR following NAC (p=0.044). Across all subtypes, patients who achieved pCR had a longer DFS than patients who did not; however the benefit of pCR was not statistically significant. pCR only improved OS and DFS in the TN disease subtype (p=0.022 and P=0.048, respectively).

Conclusion : In conclusion, pCR following NAC may have prognostic value in TN breast cancer.

PO04-02

THERAPEUTIC EFFECT OF PRIMARY SYSTEMIC CHEMOTHERAPY FOR TRIPLE NEGATIVE BREAST CANCER PATIENTS

Takashi Morimoto, Takashi Nomura

Dept. of Breast Surgery, Yao Municipal Hospital, Japan

Background/Purpose : There is a large difference in prognosis of triple negative (TN) patients and effects of chemotherapy. We evaluate the effects of primary systemic chemotherapy (PST) and prognosis for triple negative breast cancer patients.

Methods : TN is defined as ER<1% , PgR<1% and HER2 status, 0, 1+ or Fish(-) in this study. From May 2006 to June 2011, TN patients received PST followed by primary breast surgery. All patients received 4 cycles FEC and 4 cycles docetaxel or 12 cycles weekly paclitaxel before surgery. Pathological effect is defined as follows, grade 0, no effect; 1a, effects are shown under 1/3 area; grade 1b, 1/3 to 2/3; grade 2a, over 2/3 but not pCR; grade 2b, near pCR; grade 3, pCR.

Results : Twenty six patients received PST followed surgery. Of 8 patients relapsed and died within two years (group R). Other 18 patients have no relapse and are alive. (group S) Clinical response is one complete response, 14 partial response and three no change in group S and five partial response and three no charge in group R. Pathological effect is one grade two, 2 grade 1a, four grade2a in group R and one grade 1a, three grade 1b, nine grade 2a, two grade 2b, three grade 3 in group S. Good chemotherapy effect may be concerned to good prognosis as reported before. However, a half of group R showed good pathological effect (four grade 2a). Four of eighteen in group S showed not so good pathological effect (one grade 1a, three grade 1b).

Conclusion : This is very small size analysis in a single hospital. There is difficulty to expect the prognosis by clinical and pathological effect clearly in clinical practice.

PO04-03

CURRENT PRACTICE OF PERFORMING SENTINEL NODE BIOPSY AMONG CLINICALLY NODE-NEGATIVE PATIENTS AFTER NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER WITH AXILLARY NODE METASTASIS: A SURVEY CONDUCTED AMONG BREAST SURGEONS OF THE KOREAN BREAST CANCER SOCIETY

Heeseung Park[1], Jong Han Yu[1], Hee Jung Kim[1], Byung Joo Chae[2], Yongsik Jung[3], Hyun Jo Youn[4], Seho Park[5], So-Youn Jung[6], Eun-Kyu Kim[7], Jeong Eon Lee[8], Byung Ho Son[1*]

[1] *Dept. of Surgery, Univ. of Ulsan, ASAN Medical Center, Korea*
[2] *Dept. of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*
[3] *Dept. of Surgery, School of Medicine, Ajou Univ., Korea*
[4] *Dept. of Surgery, Chonbuk National Univ. Hospital, Korea*
[5] *Dept. of Surgery, College of Medicine, Yonsei Univ., Korea*
[6] *Dept. of Surgery, National Cancer Center, Korea*
[7] *Dept. of Surgery, Korea Institute of Radiological & Medical Sciences, Korea Cancer Center Hospital, Korea*
[8] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : In the current era of sentinel node biopsy (SNB) performed for clinically node-negative breast cancer in the adjuvant setting, the feasibility of performing SNB after neoadjuvant chemotherapy is of some concern. A survey was conducted among breast surgeons of the Korean Breast Cancer Society (KBCS) in order to evaluate the current practice of performing sentinel node biopsy in clinically node-negative patients after neoadjuvant chemotherapy performed for breast cancer with axillary node metastasis.

Methods : A questionnaire was sent by E-mail to breast surgeons of the KBCS. The questionnaire consisted of a case presentation and brief questions regarding sentinel node biopsy as follows: <Case presentation> A 45-year-old woman was diagnosed with right breast cancer. Core-needle biopsy confirmed invasive ductal carcinoma. The tumor size was 4cm, as seen on imaging examination. Fine needle aspiration examination for axillary lymph node enlargement showed metastatic carcinoma. However, PET / CT did not show any systemic metastasis. The patient underwent neoadjuvant chemotherapy during which the tumor size decreased by 2cm, and axillary lymph node enlargement was not observed on either palpation or imaging examination. Finally, the patient underwent breast-conserving surgery.
Question 1> Would you perform SNB on this patient?
Question 2> If you performed SNB on this patient and there was no axillary node metastasis, would you perform additional axillary lymph node dissection (ALND)?

Results : Of the total 71 respondents, the age distribution consisted of 30 (42.3%) patients below 40 years of age, 26 (36.6%) 40-49 years, 12 (16.9%) 50-59 years, and three (4.2%) over 60 years of age. In terms of the respondents' medical institutions, 57 (77.5%) worked at academic hospitals and 16 (22.5%) worked at general hospitals. For the first question, 38 (53.5%) respondents performed "SNB," while 33 (46.5%) performed "ALND." For the second question, 38 (53.5%) respondents se

lected “Additional ALND”, while 27 (38%) opted for “No additional ALND” six (9%) chose “other or no response”.

Conclusion : This survey shows that the current practice regarding SNB among clinically node-negative patients following neoadjuvant chemotherapy for breast cancer with node metastasis, varies from surgeon to surgeon in Korea. A prospective randomized clinical trial is needed in order to evaluate the clinical outcome of SNB compared to conventional ALND among patients who manifested with clinically node-negative disease following neoadjuvant chemotherapy for breast cancer patients with axillary node metastasis.

PO04-04

FACTORS FOR PREDICT THE FEASIBILITY OF SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER WITH FNA-PROVEN AXLLLARY LYMPH NODE METASTASIS, AFTER NEOADJUVANT CHEMOTHERAPY

Yura Lee

Dept. of Surgery, ASAN Medical Center, Korea

Background/Purpose : Axillary lymph node dissection (ALND) is standard method for treat axillary lymph node (ALN) metastasis of breast cancer (BC) before and/or after neoadjuvant chemotherapy (NAC), but it has well-known comorbidity like nerve injury or arm swelling. Though more and more locally advanced BC patients go through NAC, defining nodal status after NAC is still difficult. As it is still controversial to carry out SLNB in clinical lymph node (LN) positive patients after NAC, we tried to find out some clues to avoid ALND.

Methods : From October 6th 2011 to February 7th 2013, 60 locally advanced breast cancer patients in Asan medical center were enrolled prospectively. All patients had positive LN proved metastasis by ultrasound-guided fine needle aspiration cytology before NAC, and showed clinical partial response (PR) or complete remission (CR) to NAC. They had SLNB followed by ALND. To make up for the feasibility of SLNB, we sampled clinically suspected (matted, enlarged) LNs simultaneously with SLNB during the operation. After operation, we checked identification rate (IR) and false negative rate (FNR) of SLNB and SLNB with LN sampling from the final pathology reports.

Results : In this study, IR of SLNB was 78.3%(47/60) and FNR was 24.1%(7/29). In the SLNB with LN sampling, 4 patients had false negative result (FNR=13.8%). The predictive value for pathologic CR (PVpCR) was 72.0% and in SLNB with LN sampling, it was 81.8%. 33 patients had low grade BC before NAC and their IR was 75.8%, FNR was 26.3% and considering SLNB with LN sampling, FNR was 21.1%. PVpCR of SLNB was 54.5% and with LN sampling, it was 60.0%. 27 patients had high grade BC and their IR was 81.5%, FNR was 20.0% and considering SLNB with LN sampling, FNR was 0.0%. PVpCR of SLNB was 85.7% and with LN sampling, it was 100.0%. 47 patients were found metastasis only in ALN (cN1 or cN2a) before NAC and their IR was 78.7%, FNR was 26.3% and considering SLNB with LN sampling, FNR was 10.5%. PVpCR of SLNB was 78.3% and with LN sampling, it was 90.0%. Patients suspected SCLN and/or IMLN metastasis (cN3) were 13 and their IR was 76.9%, FNR was 20%, and there was no additional benefit of LN sampling. In cN3 patients, none of 13 patients was found to have pCR.

Conclusion : As the previous studies, SLNB after NAC also showed low IR and high FNR in this study. But SLNB with LN sampling would be potent method to lower FNR and improve PVpCR. SLNB may be useful to avoid unnecessary ALND in patients with high grade BC and cN1 or cN2a status, not in patients with LN metastasis beyond ALN. Due to the small number of enrolled patients in this study, further study will be needed to validate the feasibility.

PO04-05

OUTCOMES OF BREAST-CONSERVING SURGERY WITH OR WITHOUT RADIATION THERAPY IN ROUTINE CLINICAL PRACTICE

Tsuyoshi Ohno[1*], Michi Morita[1], Maiko De Kerckhove[2], Keiji Inoue[1], Masashi Haraguchi[1], Masachika Kitajima[1], Shinichiro Ito[1], Hirotaka Tokai[1], Takayuki Tanaka[1], Kazunori Minami[3], Toshio Fukuda[3], Junji Irie[4]

[1] *Dept. of Surgery, Nagasaki Municipal Hospital, Japan*
[2] *Education Research Center, Nagasaki Municipal Hospital, Japan*
[3] *Dept. of Radiology, Nagasaki Municipal Hospital, Japan*
[4] *Dept. of Pathology, Nagasaki Municipal Hospital, Japan*

Background/Purpose : The aim of this study was to elucidate the factors that influence the recurrence and prognosis of breast cancer in patients who underwent breast-conserving surgery in routine clinical practice.

Methods : Two hundred fifty-one patients who underwent BCS from January 2000 to June 2011 at our institution were identified and evaluated for risk factors for the overall survival, breast cancer death, breast cancer recurrence, ipsilateral local recurrence, regional recurrence and distant metastasis.

Results : The mean age at surgery was 59.3±12.8 years, the mean tumor size was 15.2 ± 10.2 mm and the number of node-positive patients was 44 (17.2%). Positivity for estrogen receptor expression was noted in 202 patients (80.5%), and 68 patients (27.1%) did not undergo radiotherapy. Ipsilateral breast recurrence developed in eight cases (3.2%) and regional recurrence (which included ipsilateral recurrence and axillary and supra- or subclavicular lymph node recurrence) was noted in 10 cases (4.0%). Distant metastasis occurred in 11 cases (4.4%). In total, there were 23 cases (9.2%) of breast cancer recurrence, and six cases (2.4%) of breast cancer-related death, with an overall mortality of 15 cases (6.0%). The multivariable analysis demonstrated that radiation therapy was associated with a decreased risk of ipsilateral recurrence, regional recurrence and overall mortality, and that node positivity was associated with an increased risk of breast cancer recurrence and distant metastasis, while ER positivity was associated with a decreased risk of breast cancer-related death.

Conclusion : The use of radiation therapy after breast-conserving surgery decreased the risk of local recurrence and overall mortality in routine clinical practice.

PO04-06

LUNG INJURY AFTER INTENSITY-MODULATED RADIOTHERAPY FOR BREAST CANCER

Haeyoung Kim, Hoonsik Bae*, Me-Yeon Lee, Kwang-Ho Cheong, Kyoung Ju Kim, Taejin Han, Sei-Kwon Kang, Soah Park, Taejin Hwang, Jai-Woong Yoon

Dept. of Radiation Oncology, Hallym Univ. Sacred Heart Hospital, Korea

Background/Purpose : To assess frequency, timings of occurrence, and predictors of radiologic lung damage after forward-planned intensity-modulated radiotherapy (FIMRT) for whole breast irradiation.

Methods : We retrospectively reviewed medical records of 157 breast cancer patients and each of their serial chest computed tomography (CT) taken 4, 10, 16, and 22 months after completion of breast radiotherapy (RT). FIMRT was administered to whole breast only (n=152), or whole breast and supraclavicular regions (n=5). Dosimetric parameters, such as mean lung dose and lung volume receiving more than 10-50 Gy (V10-V50), and clinical parameters were analyzed in relation to radiologic lung damage.

Results : In total, 104 patients (66.2%) developed radiologic lung change after whole breast FIMRT. Among the cases of lung change, 84.7% were detected at 4 months, and 15.3% at 10 months after completion of RT. More patients of 44 or younger were found to have lung damage at 10 months after RT than patients older than the age (16.3% vs. 5.8%, p=0.01). In univariate and multivariate analyses, age ≤ 44 years and V40 ≤ 7.2% were significant predictors for lower risk of radiologic lung injury.

Conclusion : Radiologic lung changes were not infrequently detected in follow-up CT after whole breast FIMRT. More detected cases of lung change among younger patients are believed to have developed at later points after RT than those of older patients. Age and V40 were significant predictors for lung injury after whole breast IMRT.

PO04-07

ETOPOSIDE PLUS CISPLATIN COMBINATION THERAPY IN PATIENTS WITH ADVANCED BREAST CANCER PRETREATED WITH ANTHRACYCLINES

Byonghyon Ahn, Jinsun Lee, Jeryong Kim, Eilsung Chang*

Dept. of Surgery, Chungnam National Univ. Hospital, Korea

Background/Purpose : Purpose of this study was etoposide plus cisplatin combination is effective second line chemotherapy regimen in the treatment of advanced breast cancer patients pretreated with anthracyclines.

Methods : From January 2011 to March 2013, 26 patients were enrolled. The doses of etoposide and cisplatin were 100 mg/m^2 intravenously for 3 days and 70 mg/m^2 intravenously for 1day. Treatments were repeated every 3 weeks. Response to treatment was evaluated every 6 weeks.

Results : The response rate was 38.5%. Median response duration was 5 months. Time to progression was 3.5 months. Neutropenia and nausea were acceptable toxicity.

Conclusion : Etoposide plus cisplatin combination show observed activity and acceptable toxicity. This study shows the efficacy of this relatively old treatment when compared to the new active drugs in advanced breast cancer.

PO04-08

PHASE II CLINICAL TRIAL OF IRINOTECAN COMBINED TEGAFUR-GIMERACIL-OTERACIL POTASSIUM IN METASTATIC BREAST CANCER

Hiroko Otsuka[1], **Uhi Toh**[1], **Nobutaka Iwakuma**[1], **Mai Mishima**[1], **Miki Takenaka**[1], **Ryuji Takahashi**[1], **Keiko Ueda**[1], **Shino Nakagawa**[2], **Maki Tanaka**[3], **Kazuo Shirouzu**[1]

[1] *Dept. of Surgery, School of the Medicine, Kurume Univ., Japan*
[2] *Dept. of Breast Surgery, National Hospital Organization Kyushu Medical Center, Japan*
[3] *Dept. of Surgery, Social Insurance Kurume Daiichi Hospital, Japan*

Background/Purpose : We investigated the efficacy and safety of phase II trial of irinotecan (CPT-11) combined tegafur-gimeracil-oteracil potassium (S-1) in patients with metastatic breast cancer (MBC), and the association between irinotecan metabolizing enzyme UDP-glucuronosyltransferase 1A1 (UGT1A1) gene polymorphisms and adverse events.

Methods : The study group comprised 40 patients aged 35-79 years. Irinotecan (60 mg/m^2) was administered by infusion on days 1, 8, and 15 every 4 weeks. S-1 was administered at 80 mg/m^2/day orally on days 3-7, 10-14, and 17-21 every 4 weeks.

Results : Tumor response data were available for 34 patients. Median follow-up was 12 months (range, 1-45 months). Response rate was 47% (one complete and 15 partial responses). Stable disease was observed in 17 patients (50%). One patient had disease progression (3%). Median progression-free survival was 14 months (95% CI, 10-26). Median overall survival was 26 months (95% CI, not calculable owing to sample size), and 79.3% of patients survived for 1 year. The most common grade 3 or 4 adverse events were neutropenia (15%), leukopenia (12.5%), diarrhea (7.5%), and anemia (2.5%). Treatment-related toxicity was generally modest and manageable. No significant correlation was observed between UGT1A1 polymorphisms and hematological or non-hematological toxicities.

Conclusion : This study showed the regimen using low dose CPT-11 combined S-1 was effective in MBC patients. Adverse effects were mild and this metronomic chemotherapy might be safely administered without identifying UGT1A1 polymorphisms.

PO04-09

CLINICAL OUTCOMES IN RELATIONSHIP WITH THE LINES OF CHEMOTHERAPY IN METASTATIC BREAST CANCER PATIENTS

In Hae Park[1], **Keun Seok Lee**[1], **Chan Wha Lee**[2], **Jungsil Ro**[1*]

[1] *Center for Breast Cancer, National Cancer Center, Korea*
[2] *Dept. of Radiology, Center for Diagnostic Oncology, National Cancer Center, Korea*

Background/Purpose : There is a paucity of data regarding the effect of chemotherapy beyond the 1st line in MBC patients, though many more chemotherapeutic drugs have been introduced. In this study, we assessed the effect of chemotherapies on clinical outcomes in patients with HER2 negative MBC.

Methods : We included 250 patients who were prospectively enrolled into clinical trials receiving cytotoxic chemotherapies for HER2 negative MBC at the National Cancer Center, Korea from October 2002 to December 2012. Clinicopathologic data were collected for the analysis.

Results : A total of 250, 217, and 172 patients received a first, second, and third line of chemotherapy, respectively. The median age was 49 years (range, 28-77 years) and the majority was hormone receptor positive (n=118, 74%). Median PFS was 7.4 mo for 1st line (PFS1) vs. 5.0 mo for 2nd line (PFS2) vs. 3.6 mo for 3rd line (PFS3). PFS of previous chemotherapy significantly affected subsequent PFS (PFS1 ≥ 7.4 mo, HR=0.627, 95% CI=0.473-0.829, P=0.001 in 2nd line PFS; PFS2 ≥ 5.0 mo, HR=0.642, 95% CI = 0.467-0.882, P=0.006 in 3rd line PFS). The median overall survival (OS) was 31.2 mo (range, 1.2 to 126 mo). Hormone receptor positivity (39.6 mo vs. 20.4 mo; HR=0.529) and PFS1 ≥ 7.4 mo (44.4 mo vs. 18.0 mo; HR=0.366) were significant factors for survival in multivariate analysis.

Conclusion : The efficacy of previous treatment significantly affected the outcomes of following treatment. We confirmed the succession of chemotherapy was justified in MBC patients who received benefits from the previous chemotherapy.

PO04-10

CHARACTERIZATION OF DURABLE RESPONDER FOR CAPECITABINE MONOTHERAPY IN PATIENTS WITH ANTHRACYCLINE - AND TAXANE - PRETREATED METASTATIC BREAST CANCER

Jung Yong Hong, Yeon Hee Park, Moon Ki Choi, Hyun Ae Jung, Jin Seok Ahn, Young Hyuck Im*

Dept. of Hematology-Oncology, Samsung Medical Center, Korea

Background/Purpose : Capecitabine monotherapy is effective and well tolerated for metastatic breast cancer (MBC) patients. The primary purpose of this study is to evaluate the efficacy of capecitabine monotherapy in heavily treated patients with metastatic breast cancer.

Methods : Between December 2000 and May 2012, a total of 236 evaluable patients with MBC were included who had been treated with second or more line of palliative capecitabine monotherapy after previous treatment history with anthracycline and taxane containing regimen. Capecitabine (1,250 mg/m^2 twice daily) was administered for 2 weeks followed by a 1-week rest period.

Results : The response rate was 23.5% and median PFS was 4.7 months (95% CI; 4.0-5.5). Among 236 patients, 33 patients (14.0%) showed durable response (>12 months) to capacitabine monotherapy. Patients with durable response (DR) group showed significantly higher incidence of estrogen receptor (ER) positivity (81.8% vs. 59.1%, P=0.012), single organ metastasis (51.5% vs. 32.0%, P=0.047), absence of lymph node (LN) metastasis (75.8% vs. 54.2%, P=0.023), compared to patients without durable response (non-DR group). Median PFS patients with ER positivity vs. negativity, single vs. two or more metastasis, and absence vs. presence of LN metastasis were as followings; 6.9 vs. 3.6 months (P<0.001), 5.5 vs. 4.3 months (P=0.005), and 4.9 vs. 4.3 months (P=0.018), respectively. In the multivariate analysis, ER positivity and single organ metastasis retained significant association with better PFS to capecitabine monotherapy (hazard ratio [HR] of 0.51, P<0.001 and HR of 0.62, P=0.004).

Conclusion : Our data suggest that ER positivity and single organ metastasis can be useful predictive markers for better PFS to second or more line of palliative capecitabine monotherapy in anthracycline- and taxane ?pretreated MBC patients.

PO04-11

EFFICACY OF GEMCITABINE/CISPLATIN CHEMOTHERAPY IN CORRELATION WITH CLINICAL CHARACTERISTIC IN ANTHRACYCLINE - AND TAXANE - PRETREATED METASTATIC BREAST CANCER PATIENTS

Jung Sun Kim[1], **Jung Sil Ro**[2*], **In Hae Park**[2]

[1] *Dept of. Hemato-Oncology, Korea Univ. Medical Center, Korea*
[2] *Dept. of Oncology, Center for Breast Cancer, National Cancer Center, Korea*

Background/Purpose : While metastatic breast cancer (MBC) is regarded as an incurable disease, there is no standard therapeutic option in MBC patients who were progressed on anthracycline and taxane based chemotherapies. Gemcitabine plus cisplatin (GP) have been utilized resulting in moderate activity in MBC patients. We retrospectively analyzed the efficacy of GP according to various clinical factors for the predictive and prognostic significance of GP treatment.

Methods : We included MBC patients who received GP in up to the third line metastatic setting from Jan. 2001 to Nov. 2011 at the National Cancer Center, Korea. Patient clinical and pathologic data were collected.

Results : Of 384 patients initially included, data on 294 eligible patients were analyzed for the study. All patients had been treated by taxane and anthracycline either in adjuvant or in palliative setting (GP in 1st line; 4.1%, 2nd line ; 21.8%, 3rd line; 40.6%). The median age was 48 years (range, 28 to 78 years) and the median progression-free survival (PFS) of patients receiving GP was 4.2 months (95% CI, 0.1 to 24.5 months). Significant predictive factors for PFS by GP were ECOG ≥2 (HR=1.37; 95% CI 1.02-1.85, p=0.03), distant disease free interval (DDFI) (≤2 years vs. > 2 years, HR=1.66; 95% CI 1.28-2.15, p<0.001), time interval from the diagnosis of metastasis to the start of GP therapy (TTGP) (≤1year vs. >1year, HR=1.48, 95% CI 1.13-1.95, p<0.001), and the presence of brain metastasis (HR=1.47, 95% CI 1.13-1.95, p=0.005). All of these factors remained as significant after multivariate analysis. DDFI (≤2 years vs. >2 years, HR=2.06; 95% CI 1.36-3.13, p<0.001) and the presence of brain metastasis (HR=2.14, 95% CI 1.27-3.61, p=0.004) were associated with survival after GP treatment.

Conclusion : GP chemotherapy is an effective treatment option for heavily pretreated MBC patients.

Total	294	
Age (years, median, range)	48 (28-78)	
≤50YA	173	59%
>50YA	121	41%
DDFI (years, median, range)	3.1 (0-16.4)	
Time interval from a diagnosis to the start of GP therapy (TTGP) (months, median, range)	24.1 (0-105.1)	
GP 종료이유		
Ongoing	14	4.8%
PD	217	73.7%
>PR	5	1.7%
AEs	17	5.8%
Death	9	3.1%
Others*	32	10.9%
Receptor status (HR/HER2)		
HR(+)/HER2(-)	138	47.1%
HR (±) /HER2(+)	80	27.0%
Triple-negative	76	25.9%
Metastatic sites		
Bone	159	53.9%
Brain	47	15.7%
Visceral	210	71.3%
Number of prior chemotherapies for MBC		
0	12	4.1%
1	64	21.8%
2	119	40.6%
3	99	33.4%
Hormone therapy for MBC	131	44.7%
Adjuvant chemotherapy	226	77.1%
ECOG		
0	13	4.4%
1	205	70.0%
2	73	24.6%
3	3	1.0%

Table 1

	HR for PFS (Univariate)	P value	HR for PFS (multivariate)	P value
ECOG (2,3 vs 0,1)	1.32 (0.99-1.76)	0.05	1.37 (1.02-1.85)	0.03
Age (>50YA vs ≤50YA)	1.06 (0.81-1.38)	0.65	-	-
Number of prior chemotherapies (2,3 vs 0,1)	1.14	0.36	-	-
Receptor status (HR/HER2)			-	-
HR(+)/HER2(-)	1.0			
HR (±) /HER2(+)	1.19 (0.89-1.59)	0.23		
Triple-negative	1.16 (0.86-1.55)	0.32		
DDFI (≤ 2yrs vs > 2 yrs)	1.79 (1.39-2.31)	0.000	1.66 (1.28-2.15)	0.000
TTGP (≤1YA vs > 1YA)	1.67 (1.28-2.18)	0.000	1.48 (1.13-1.95)	0.005
Metastatic sites			-	-
Bone	1.03 (0.80-1.33)	0.79	-	-
Brain	1.45 (1.03-2.04)	0.02	1.47 (1.03-2.10)	0.03
Visceral	1.14 (0.86-1.51)	0.35		

Table 2

PO04-12

EFFICACY OF PACLITAXEL PLUS BEVACIZUMAB COMBINATION THERAPY FOR METASTATIC BREAST CANCER

Tsutomu Takashima[1*], **Hidemi Kawajiri**[1], **Satoru Noda**[1], **Shinichiro Kashiwagi**[1], **Tamami Morisaki**[1], **Mao Watanabe**[1], **Yukie Go**[1], **Yuka Asano**[1], **Sae Ishihara**[1], **Taeko Nakano**[2], **Yasuko Mitsukawa**[3], **Noriko Kawakami**[3], **Naoyoshi Onoda**[1], **Kosei Hirakawa**[1]

[1] *Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan*
[2] *Dept. of Nursing, Osaka City Univ. Hospital, Japan*
[3] *Dept. of Pharmacy, Osaka City Univ. Hospital, Japan*

Background/Purpose：Combination therapy of paclitaxel and bevacizumab (PTX+Bv) showed very high response rate and prolongation of progression free survival compared with paclitaxel monotherapy as a first line chemotherapy for metastatic breast cancer in E2100 trial. However, this regimen could not contribute for prolongation of overall survival. Bevacizumab was approved for treatment of metastatic breast cancer with paclitaxel on September 2011 in Japan. Although PTX+Bv has no benefit for overall survival, it is fast-acting and has extremely high response rate. This character of the combination therapy is suitable for treatment of so-called life threatening visceral metastasis, symptomatic lesion and rapid growing tumor in significance to escape from these critical situations. We used PTX+Bv (paclitaxel 90 mg/m^2 weekly for 3 consecutive weeks and 1 week rest, bevacizumab 10 mg/kg biweekly) for 24 cases who have life threatening lesion or rapid growing tumor from October, 2011 through June, 2013. Herein, we report our experience of this regimen.

Methods：All cases were women and has a HER2-negative tumor. Patients' age were 31-79 (median 54) years old. Eighteen cases were ER-poisitive and 6 cases were ER-negative. They received 0-9 prior chemotherapies (median, 2 regimens).

Results：The patients received 1-16 cycles of PTX +Bv (median 4 cycles). Overall response were CR 0, PR 15(62.5%), SD 7 (29.2%), PD 2 (8.3%). Mean time to failure was 14 weeks and mean survival time was 48 weeks.

Conclusion：PTX+Bv is fast-acting and may show good response even in late line of the treatment. It seems that this regimen should consider use for a life threatening or rapid growing lesion.

PO04-13

CBT-143, AN ETHANOL EXTRACT FROM JUNIPERUS CHINENSIS, POTENTIALLY APPLIED IN BREAST CANCER TREATMENT THROUGH ANTI-ANGIOGENESIS AND TUBULIN INHIBITION

Mei-Wei Lin*, I-Horng Pan, Ching-Huai Ko, I-Huang Lu, Hsin-Jan Yao, Hsin-Chieh Wu, Zong-Keng Kuo, Hsiang-Wen Tseng, Nien-Tzu Chou

Biomedical Technology and Device Research Laboratories, Industrial Technology Research institute, Taiwan

Background/Purpose：Breast cancer is the most lethal disease in Western women and more than one million global cases of breast cancer were diagnosed each year. Distant organ metastasis accounts for 90% deaths of breast cancer and inhibiting angiogenesis of breast cancer could be one critical step to control tumor spreading. In this study, we investigate the efficacy of CBT-143, an ethanol extract of Juniperus Chinensis in targeting tumor proliferation and tumor-associated angiogenesis.

Methods：Alarma Blue assay was used to observe cell growth of human umbilical vein endothelial cells (HUVEC), breast cancer cell lines, and peripheral blood mononuclear cells (PBMC) treated with different concentration of CBT-143. Anti-angiogenesis activity of CBT-143 was evaluated by in vitro cellular assays (proliferation, migration, tube formation) and in vivo matrigel plug and chick chorioallantoic membrane (CAM) assay. Tubulin polymerization assay was conducted to study the assembly and depolymerization of tubulin after CBT-143 treatment. For assessment of apoptosis, the cells were stained with Annexin V and propidium iodide and evaluated with flow cytometer. Orthotopic MDA-MB-231 mouse xenograft models were used to assess the effects of CBT-143 on tumorigenesis.

Results：CBT-143 significantly inhibited migration and capillary tube formation of HUVEC at very low dose (<0.1 μg/mL). CBT-143 treatment both inhibited the growth of HUVEC and breast cancer cell by G2/M phase arrest. And tubulin depolymerization is also involved in the CBT-143 mediated growth inhibition. Additionally, anti-angiogenesis activity of CBT-143 could be reversed by TPA but not 4-alpha TPA, this result suggested that PKC play a critical role in anti-angiogenesis activity of CBT-143.

Conclusion：Bevacizumab (anti-angiogenesis antibody) and paclitaxel (tubulin inhibitor) are sometimes suggested to be used together to treat metastatic breast cancer clinically. In this study, we suggest CBT-143, a dual-function agent that blocks angiogenesis and microtubule assembly, shows potential effect in inhibiting capillary tube formation in HUVEC and inducing apoptosis in breast cancer cells. Therefore, CBT-143 is considered as a potential therapeutic agent in breast cancer treatment based on our investigation.

PO04-14

USEFULNESS OF FULVESTRANT FOR POSTMENOPAUSAL METASTATIC BREAST CANCER

Satoru Noda, Yuka Asano, Yukie Go, Mao Watanabe, Tamami Morisaki, Shinichiro Kashiwagi, Hidemi Kawajiri, Tsutomu Takashima, Naoyoshi Onoda*, Kosei Hirakawa

Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan

Background/Purpose : Selective estrogen receptor modulators (tamoxifen, toremifene), aromatase inhibitor, acetic acid medroxyprogesterone, and fulvestrant are considered available for endocrine therapy after initial failure of the therapeutic effort for postmenopausal metastatic breast cancer with positive hormone receptor, still the optimal indications of each drugs are not clear. In this study we reported our experience of therapy with fulvestrant.

Methods : All cases are woman with metastatic breast cancer receiving fulvestrant therapy from November 2011 to July 2013. The average age was 63 years old (41-87 years old). Fulvestrant was administered by high does regimen. The dose was 500 mg at intervals of one month, with an additional 500 mg dose given two weeks after the initial dose.

Results : No case had the effect of complete response (CR), four cases had that of partial response (PR), eight cases had that of stable disease (SD), and 16 cases had that progressive disease (PD). Objective response rate (ORR; CR+PR) was 14.3%, and clinical benefit rate (CBR; PR+SD > 24 weeks) was 32.1%. CBR of the cases showed CB by previous endocrine therapy was 42.1 %, but CBR was 11.1 % in cases who did not respond to the previous endocrine therapy. CBR of fulvestrant treatment was as high as 43.8% when applied as fourth line therapy or later, however that was only 16.7 % for the second or the third line. The median progression free survival (PFS) was three months in all patients. PFS of the patient with previous effective endocrine therapy was four months, and it was significantly longer compared with that of two months in the patients without previous effective therapy. PFS was significantly longer (six months) in cases administered fulvestrant as fourth line or later, compared with that (three months) in cases applied as second or third line.

Conclusion : Fulvestrant was effective for a case to achieve an effect for endocrine therapy by previous treatment, and it was suggested that fulvestrant was effective for late line of endocrine therapy.

PO04-15

THE OBJECTIVE COSMETIC RESULTS AND PATIENT REPORTED OUTCOMES OF LATISSIMUS DORSI FLAP ONCOPLASTIC SURGERY

Zisun Kim[1], **Sang Gue Kang**[2], **Sung Yong Kim**[1], **Cheol Wan Lim**[1], **Min Hyuk Lee**[1*]

[1] *Dept. of Surgery, Soonchunhyang Univ. Hospital, Korea*
[2] *Dept. of Plastic and Reconstructive Surgery, Soonchunhyang Univ. Hospital, Korea*

Background/Purpose : The goal of oncoplastic breast surgery is to maintain and restore the appearance of the breast and to improve patient satisfaction after caner ablation. Thus, the assessment of cosmetic results and patient reported outcomes (PRO) using appropriately constructed and validated instruments is essential to evaluate and qualify the success of these surgeries from the patient's perspective. The aim of present study was to assess the objective cosmetic results and PRO of latissimus dorsi (LD) flap oncoplastic surgery using an appropriate and validated measurement tool.

Methods : The cosmetic results were assessed by three different groups; patient, a panel of medical team (2 breast surgeons, 2 plastic surgeons, 2 nurses, and 2 aid nurses), and a software reported to objectively measure the cosmetic outcomes (BCCT.core). The patient satisfaction was assessed by the BREAST-Q, which is a specific questionnaire related to breast surgery. The cosmetic results among the 3 groups were compared, and the PRO was analyzed in a cohort of 63 consecutive breast cancer patients who underwent partial breast reconstruction using LD flap.

Results : The mean age of the patients was 51 years old (range, 33-72). Stage distribution of the patients was; stage 0 in 6 patients, stage I in 29, stage II in 25, and stage III in 3. The mean tumor size was 2.1cm (range, 0.8-5.5cm). A total of 57 patients (90.2%) were satisfied with the cosmetic results, and 29 (46.0%) replied their cosmesis as excellent. Compared to the BCCT.core, patients and the medical team had a tendency to score the cosmetic results nicer. On a linear regression analysis, the BCCT.core results and the BREAST-Q showed a positive correlation regarding to satisfaction with breasts (ß=6.4, p=0.039), satisfaction with outcome (ß=7.3, p=0.021), psychosocial well-being (ß=6.6, p=0.023), and sexual well-being (ß=7.7, p=0.041).

Conclusion : The overall patient satisfaction was high after LD oncoplastic surgery, and the objective cosmetic results reflected the PRO well. The strengths of this study include the use of valid, reliable, procedure-specific cosmetic and PRO measures. And this is the first report to prove the correlation of objective cosmetic results with subjective patient satisfaction after oncoplastic breast surgery.

PO04-15

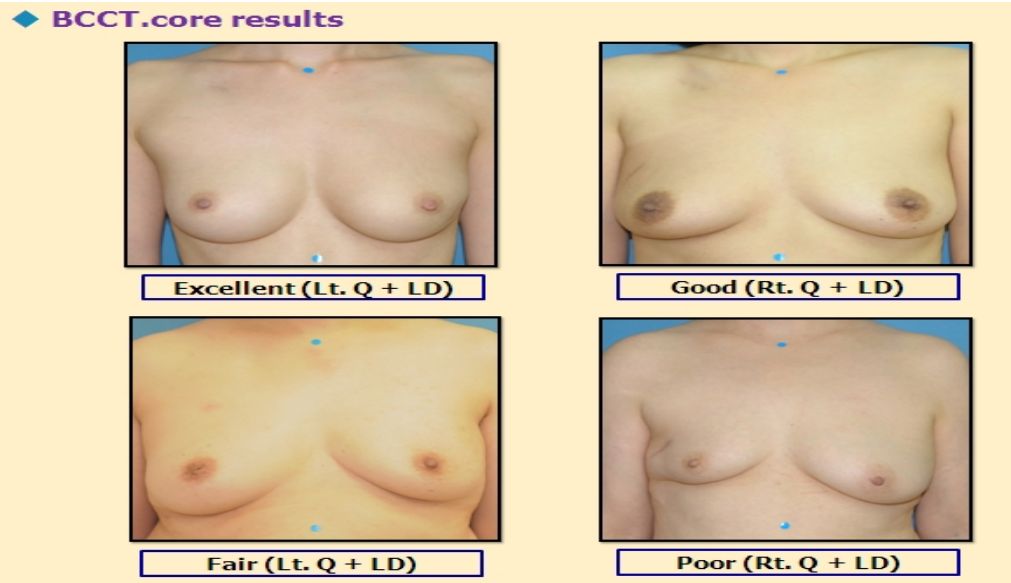

Figure 1

BREAST-Q Results

Domain (reconstruction module)	Mean (range), n=63
Satisfaction with breasts	64.6 (30-100)
Satisfaction with outcome	82.4 (47-100)
Psychosocial well-being	76.0 (38-100)
Sexual well-being	57.5 (0-100)
Physical well-being (chest)	68.7 (50-100)
Physical well-being (back)	62.9 (0-100)
Satisfaction with information	71.7 (41-100)
Satisfaction with surgeon	84.4 (11-100)
Satisfaction with medical team	84.6 (42-100)
Satisfaction with office team	82.9 (38-100)

Table 1

PO04-16

DISEASE RECURRENCE IN SENTINEL NODE POSITIVE BREAST CANCER PATIENTS WITH OR WITHOUT AXILLARY NODE DISSECTION

Nana Rokutanda, Jun Horiguchi, Daisuke Takata, Rin Nagaoka, Ayako Sato, Hideaki Tokiniwa, Sayaka Uchida, Misato Ogino, Izumi Takeyoshi

Dept. of Thoracic and Visceral Organ Surgery, Graduate School of Medicine, Gunma Univ., Japan

Background/Purpose : Clinically node-negative breast cancer patients usually undergo sentinel lymph node (SLN) biopsy. When metastasis is identified, axillary lymph node dissection (ALND) is recommended. The data from Z0011 suggest that ALND does not improve local control or survival of breast cancer.

Methods : Women with a positive SLN diagnosed between 2004 and 2010 were included in this study and were stratified according to whether they did or did not undergo ALND. Axillary and distant recurrence was analyzed retrospectively.

Results : Overall, 191 women were included in this study. A total of 151 patients had macrometastatic SLN disease and 40 patients had micrometastatic SLN disease. A total of 154(80.6 %) patients underwent ALND (ALND+) and 37 (19.3%) patients had no further axillary surgery (ALND-). All patients in ALND- were diagnosed pathologically as negative SLN during operation. Patients in ALND+ received more chemotherapy (P=0.0003). The groups did not vary by other characteristics. Distant recurrence occurred in five patients (3.3%) in ALND+ and three patients (8.8 %) in ALND- (P = 0.18). Nobody had axillary lymph node recurrence occurred in each group as far as the present time. So far no occurrence of axillary recurrence was noted in each group. Patient age, tumor size, histology, subtypes, HER2 status, ER status, and SLN metastasis status (micrometastatic or macrometastatic) were not associated with the recurrence. Similarly type of surgical therapy (mastectomy versus breast conserving surgery), with or without radiation, and type of adjuvant therapy showed the same recurrence disassociation.

Conclusion : As previous studies reported, the omission of ALND in patients with SLN disease does not significantly have an impact on in-breast, nodal, or distant recurrence. Longer-term follow-up is needed to verify this result.

PO04-17

EFFECT OF RADIATION THERAPY ON LOCAL CONTROL IN PATIENTS WITH POSITIVE SURGICAL MARGINS AFTER BREAST-CONSERVING SURGERY

Rin Nagaoka*, Jun Horiguchi, Daisuke Takata, Nana Rokutanda, Ayako Sato, Hideaki Tokiniwa, Toru Higuchi, Sayaka Uchida, Misato Ogino, Izumi Takeyoshi

Dept. of Thoracic and Visceral Organ Surgery, Graduate School of Medicine, Gunma Univ., Japan

Background/Purpose : The surgical margin status after breast-conserving surgery (BCS) has been associated with the risk of local recurrence. The purpose of study is to retrospectively evaluate the effect of a higher radiation dose on local control in patients with positive margins.

Methods : A total of 1,083 patients who underwent BCS followed by whole breast irradiation of 50 Gy between 1991 and 2009 were including in this study. 138 patients (13%) with positive margins were assigned to receive or not an extra boost dose of 10 Gy. A positive margin was defined as tumor seen at 5mm or less from the resection edge.

Results : At a median follow-up of 8.5 years, the rate of local recurrence was 2.1% (23/1083). Positive margin status was found to be a significant risk factor for local recurrence. For patients with positive margins, the boost dose of 10 Gy reduced the local recurrence from 23% to 2%. There was no significant difference in local recurrence rate between patients with positive margin who treated with 50 Gy and boost and those with negative margin without boost. In addition, patients with positive margin who treated with 50 Gy and boost showed no significant difference in local relapse rate compared with patients who underwent additional local resection before whole breast irradiation.

Conclusion : Our results suggest that boost irradiation to the tumor bed in patients with positive margins after breast-conserving surgery reduces local recurrence.

PO04-18

BREAST CONSERVATION IN BREAST CANCER: A BANGLADESH EXPERIENCE

Syeda Hasina Azam*

Dept. of Surgery, Euro Bangla Hospital, Bangladesh

Background/Purpose : Breast cancer is one of the most common cancers in Bangladeshi women. Breast sacrificing treatment is still the common practice in our country. Nowadays breast conservation is the standard treatment of breast cancer without compromising the survival. The purpose of this study is to have disease free and overall survival in breast cancer.

Methods : Between Jan. 1996 and Dec. 2010, breast conserving treatment had been carried out in different institutions of Bangladesh on breast cancer patients who had been diagnosed by fine needle aspiration cytology/core biopsy/incision/excision biopsy or attended immediately after breast conserving surgery. Clinical staging was recorded by physical examination, relevant investigations as well as surgical records. Revised breast conserving surgery had been done on those who had positive surgical margins or palpable disease. The patients with large but operable cancer or locally advanced cancer were treated by neoadjuvant chemotherapy followed by breast conserving surgery. Systemic adjuvant therapy (chemotherapy and or hormone therapy) and adjuvant radiotherapy was given. After completion of treatments, the patients were followed up as standard protocol and data were compiled and analysed.

Results : A total of 224 patients were treated. Characteristics of the patients; age 22- 74 years (mean age 42.35 years); pre-menopausal 75%. The patients were educated (95%), economically solvent with good performance status; T1-3N0M0 was 65%, T1-3N1M0 -30%, T4bN1M0-5 cases, T0N1-2M0-3 cases, T2-3N1M1-2 cases. The histopathology was invasive duct cell carcinoma in 98% cases and intraductal carcinoma *in situ* in 4 cases. The surgical treatment given was wide local excision/quadrantectomy/with or without axillary clearance in 158 patients. Revised breast conserving surgery was done in 53 cases and mastectomy in 8 cases. 5 cases had biopsy done only with no further surgical treatment. Chemotherapy was given in 192 patients (86%); adjuvant in 122 cases and neoadjuvant in 70 cases. Anthracycline combination was given in 115 cases, anthracycline combination with Taxane was given in 69 cases, and anthracycline combination with and Herceptin was given in 8 cases. Hormone therapy with tamoxifen or letrozole was given in 182 patients. Radiotherapy: External beam therapy 45-50 Gy and 10-12 Gy electron boost was given in all cases. Follow up period was 3 to 17 years; overall survival was 86%, disease free survival was 80% and local recurrence 4%.

Conclusion : Breast conserving treatment was satisfactory for appropriate case selection and optimized therapy. Survival was in no way worse than breast sacrificing treatment.

PO04-19

NEOADJUVANT THERAPY IS NO BAR TO METICULOUS SKIN SPARING MASTECTOMY AND COMPLEX IMMEDIATE RECONSTRUCTION

Eric Drabble*

Breast Unit, Derriford Hospital, United Kingdom

Background/Purpose：Neoadjuvant chemotherapy can bring aggressive breast tumours under control facilitating subsequent surgical therapy, including skin sparing mastectomy and reconstruction to minimise the cosmetic impact of cancer surgery. However, the adverse effects of chemotherapy could affect patients' capacity to undergo complex immediate reconstruction, increasing complications and affecting their long term outcome.

Methods：Outcomes of one surgeon's practice of 44 skin sparing mastectomies (SSM) and immediate reconstruction with tissue flaps following neoadjuvant chemotherapy in two institutions over 12 years were determined by assessing case records and electronic radiology and histology databases to detect adverse outcomes. All patients underwent biopsy of what subcutaneous fat was left following SSM.

Results：Thirty eight patients' outcomes were reviewed. 6 patients underwent bilateral SSM. Three types of reconstructions were performed, transverse rectus abdominus myocutaneous (TRAM) flap (20), latissimus dorsi flap (LD) and implant (15), extended LD flap alone (8) and one declined reconstruction. All subcutaneous flap biopsies were clear of any breast epithelial elements. No patient suffered a local recurrence. 10 patients suffered systemic recurrences. One implant required replacement. One TRAM flap was removed. One patient suffered skin necrosis requiring debridement.

Conclusion：Meticulous SSM and complex flap based reconstruction can be safely delivered after neoadjuvant chemotherapy producing good disease control, particularly local control, with minimal complications.

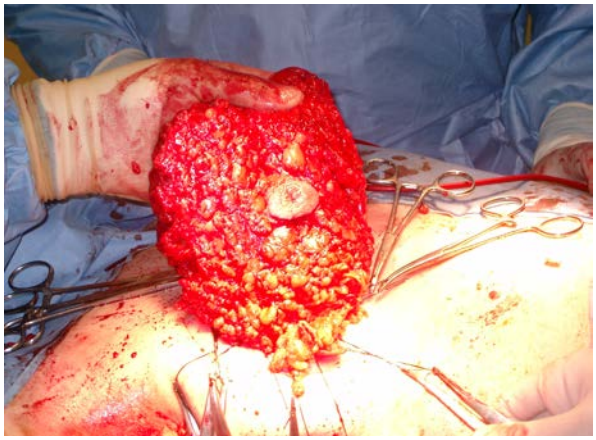

Figure 1

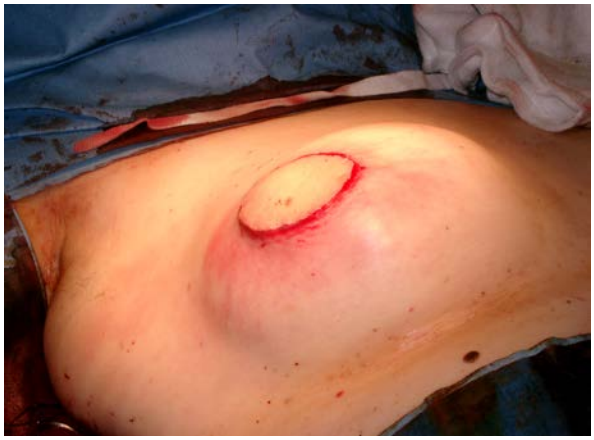

Figure 2

PO04-20

BREAST CONSERVATION SURGERY FOR MALIGNANCY VIA AN AESTHETIC APPROACH CAN BE ONCOLOGICALLY SAFE

Eric Drabble*

Breast Unit, Derriford Hospital, United Kingdom

Background/Purpose：The efficacy of breast cancer surgery is probably better reflected by the subsequent long term local recurrence rate, than systemic recurrence, and this measure was applied to the outcomes of aesthetic breast conservation surgery by one surgeon over a 12 year period.

Methods：A total of 505 such procedures were performed via periareolar incisions. Patients records and electronic databases of radiographic and histological records were interrogated to determine their outcomes.

Results：Over a median follow up period of 7 years, 8 patients (0.6%) developed a local recurrence or separate new cancer in the remaining breast, 19 (3.8%) systemic recurrence, and 38 patients were converted to mastectomy for disease related issue or patient preference (7.5%). Over 90% of patients retained their original reconstructions with no local recurrence and 95% were disease free.

Conclusion：Aesthetic breast cancer surgery via remote incisions allows safe surgical control of disease as well as retention and reformation of the breast shape via a relatively scarless approach.

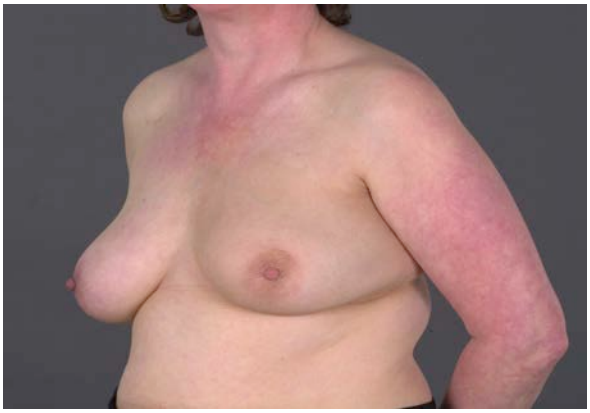

Figure 1

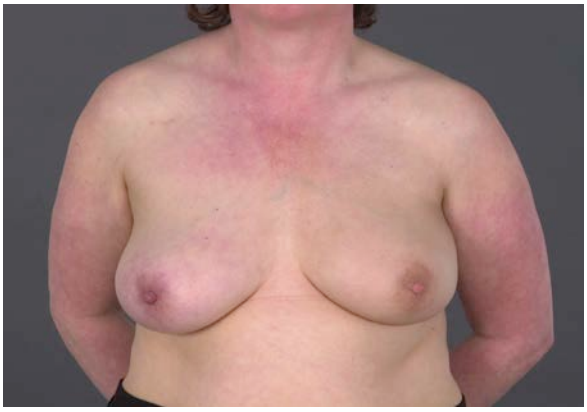

Figure 2

PO04-21

THE EXAMINATION OF POSTOPERATIVE PAIN MANAGEMENT BY INTRAOPERATIVE SUBCUTANEUS LOCAL INFILTRATION ANESTHESIA FOR BREAST SURGERY

Kazushige Futsuhara[1*], **Kojiro Suzuki**[1], **Osamu Sekine**[1], **Toshiki Rikiyama**[1], **Takanori Murayama**[2]

[1] *Dept. of Surgery, Jichi Medical Univ., Saitama Medical Center, Japan*
[2] *Dept. of Anestesia, Jichi Medical Univ., Saitama Medical Center, Japan*

Background/Purpose：Various methods for the postoperative acute pain have been used, but an effective method is not established. In the our postoperative management schedule, the patient have been going to start walking two after the breast surgery two hours, and a meal have started from the operative day. For that purpose, postoperative acute pain management is required. We introduced a method to spray a local anesthetic under the skin when a wound was closed. We examined retrospectively the effectiveness of the subcutaneous local infiltration anesthesia using the frequency of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Methods：We intended for 507 women performed breast surgery by November, 2011 from January, 2007. We classified group in 252 cases until from January, 2007 to July, 2009 before local infiltration anesthesia introduction (group A), 255 cases until from August, 2009 to November, 2011 as a group after introduction (group B). When wound have been closed, 0.75% ropivacaine 10 mL subcutaneously was sprayed (when there is an axillary incision, ropivacaine 3 mL approximately was sprayed on an axillary region).

Results：The average age is group A 58.1 (24-78), and group B 59.3 (35-87). NSAIDs was used an average of 1.639 times in the group A, and an average of 1.896 times of group B whole hospitalization, but there were not the significant difference (p=0.75862) between both groups. On the operation day, NSAIDs was used an average of 0.7073 times in the group A, and an average of 0.5167 times of group B. The use of NSAIDs significantly decreased by ropivacaine（p=0.01022）. In the cases of breast partial resection, NSAIDs was used an average of 0. 6917 times of group A and an average of 0.5054 times of group B (p=0.013319) and in the cases of drain-free, average of 0.6865 times of group A and an average of 0.4384 times of group B (p=0.03312 and p=0.013319, respectively) . Ropivacaine in particular was significantly effective in these two cases.

Conclusion：We regard that the postoperative pain management is the important factor because early rehabilitation have been started early. The local infiltration anesthesia accords at the organization, and a drug infiltrates the nerve fiber end uniformly. In addition, there is little damage of the organization in comparison with direct puncture, the procedure is simple and easy. Ropivacaine permeates pectoralis major fascia which is a cause of the pain effectively. The ropivacaine local infiltration anesthesia was effective in breast partial resection and drain-free case, but was not effective in mastectomy and the drain using case. Ropivacaine does not penetrate enough because an excision range is wide in mastectomy and ropivacaine discharge in drain using cases. The frequency of NSAIDs decreased by intraoperative subcutaneus local infiltration anesthesia, and the method was very useful for perioperative management.

PO04-22

SKIN SPARING MASTECTOMY AND BREAST RECONSTRUCTION: WE CAN PRODUCE METICULOUS LOCAL DISEASE CONTROL

Eric Drabble*

Breast Unit, Derriford Hospital, United Kingdom

Background/Purpose：Skin sparing mastectomy allows aesthetic removal of the breast and reconstruction, but could this be at the cost of retaining significant breast tissue?

Methods：Skin sparing mastectomies and reconstructions (TRAM, extended latissimus dorsi (LD), LD flap + implant and subpectoral implant) carried out by a single surgeon over a 15 year period, who regularly sampled what subcutaneous fat remained were assessed for: Histological evidence of breast epithelial elements in subcutaneous samples, local recurrence, and systemic recurrence. This was completed by interrogating the surgeon's individual database, and hospital electronic radiology and pathology databases. All the case of bar those unfit for extensive surgery, patients with inflammatory carcinomas unresponsive to neoadjuvant chemotherapy, extensive T4 disease and known metastatic disease were offered skin sparing mastectomy and reconstruction.

Results：A total of 402 skin sparing mastectomies were performed. Skin flap biopsy results were available in 357 cases. The median follow up period was 9 years. Three patients had evidence of residual breast epithelial elements, 4 patients confirmed local recurrence, 42 patients systemic recurrence. The annualised local and systemic recurrence rates were 0.11% and 1.16% respectively. The local recurrence rate over this prolonged period was <1%.

Conclusion：A meticulous approach to skin sparing mastectomy can allow very good local disease control as well as a good aesthetic outcome for all breast cancer patients without locally advanced disease requiring mastectomy.

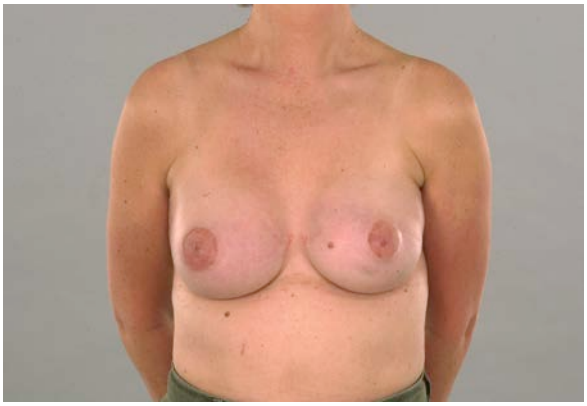

Figure 1

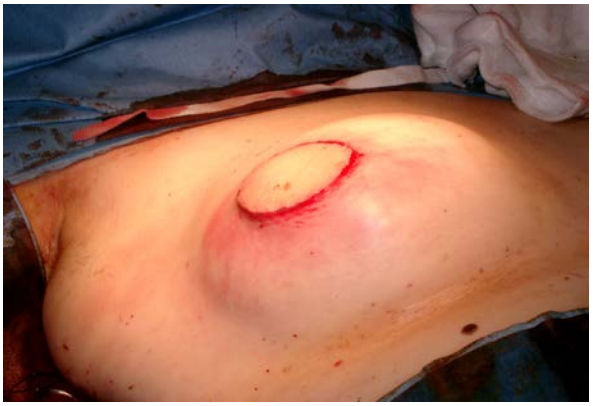

Figure 2

PO04-23

AESTHETIC OUTCOMES OF LATISSIMUS DORSI MYOCUTANEOUS FLAP WITH OR WITHOUT THE TISSUE EXPANDER AFTER MASTECTOMY FOR EARLY BREAST CANCER PATIENTS

Moonhaeng Lee, Jeryong Kim*

Dept. of Surgery, College of Medicine, Chungnam National Univ., Korea

Background/Purpose : Traditionally, in Korean women, many people were slim and had small sized breasts. But, as time goes on, some people had bigger sized breasts. The latissimus dorsi (LD) flap was conventionally thought to be a inadequate reconstruction for breast cancer patients whom had large breast. In this study, we demonstrate that the LD flap with or without the tissue expander is useful for any size of breast.

Methods : The data of 74 early breast cancer patients was reviewed retrospectively whom underwent the mastectomy with immediate breast reconstruction. 13 patients underwent reconstruction with transverse rectus abdominis musculocutaneous (TRAM) flap and 50 patients with the LD flap (with the tissue expander or without the tissue expander) and 11 patients with tissue expander alone. The aesthetic outcomes was rated as good, fair, or poor according to sum of scores of the four parameters: symmetry , breast shape , scarring, and the position of the nipple-areolar complex (NAC). And the satisfaction of patients was rated as good, fair, or poor.

Results : The mean age was 47.2 years, the average follow-up interval was 33.1 months ,and the average resected mass weight is 308g. 13 patients underwent reconstruction with TRAM flap and 50 patients with the LD flap (with the tissue expander or without the tissue expander) and 11 patients with tissue expander alone. The average resected mass weight was 354g in the TRAM flap group, 290g in the LD flap group and 247g in the implant group. Statistical analysis was done and symmetry was the most significant factor of patient satisfaction. ($p<0.001$) There was 8 cases of asymmetry in the TRAM flap (54%), 7 cases in the LD flap with the tissue expander or without the tissue expander (14%) , and 4 cases in tissue expander alone (36%). There was a statistical significance in asymmetry or aesthetic outcomes between the three groups. ($p=0.007$) Most of the patients were satisfied with the reconstruction (n=62, 84%) and 12 patients were not (16%).

Conclusion : The LD flap can be used for not only small breasts but also large breasts. Furthermore, LD flap decrease operative time while maintaining similar or superior aesthetic outcomes, so it is a feasible option for immediate breast reconstruction.

PO04-24

OUTCOMES OF DUCTAL CARCINOMA *IN SITU* TREATED WITH BREAST CONSERVING SURGERY WITH AND WITHOUT ADDITIONAL RADIOTHERAPY, A RETROSPECTIVE STUDY OF 100 CASES

Tae Ryung Kim, Kyung Hee Lee, Kwan Il Kim, Yong Soon Chun, Tae Hoon Lee, Heung Kyu Park*

Dept. of Surgery, Breast Cancer Center, Gachon Univ. Gill Hospital, Korea

Background/Purpose : Establishing a clear management for ductal carcinoma *in situ* (DCIS) has been challenging because of the heterogeneous and complex nature of this disease.

Methods : We reviewed patients with DCIS treated with breast conserving surgery with or without radiotherapy applying the van Nuys prognostic index (VNPI) score system. Of these patients, 23.7% had a low VNPI score, 61.9% intermediate and 14.4% a high score. We excluded high VNPI score group in this analysis, and reviewed 100 patients of low and intermediate VNPI score group. In the low score group, 46.4% of the patients underwent breast conserving surgery (BCS) without radiotherapy (RT) while in the intermediate group, 81.9% of patients received RT. Eighty-three percent of patients (83 out of 100) had estrogen positive tumors and all of them were received tamoxifen.

Results : Three percent of patients (3 out of 100) had developed local recurrence after median follow up period of 42 months. The recurrence was observed only in intermediate group with radiotherapy, and 2 out of 3 had ER negative tumors. Among who did not receive radiotherapy in the intermediate group, none of them experienced recurrence and 85.7% of them had ER positive tumors.

Conclusion : We did not find any statistically significant advantage in the low and intermediate groups treated with addition of radiotherapy. Additionally, in those groups, there seem to have no additional effect of radiotherapy especially to the patients with ER positive tumor. However, only prospective randomized studies can precisely predict the risk of local recurrence of BCS in DCIS.

PO04-25

OUTCOMES IN POSTMENOPAUSAL WOMEN WITH HORMONE RECEPTOR POSITIVE, HER-2 NEGATIVE T2N0 BREAST CANCER WITHOUT ADJUVANT CHEMOTHERAPY

Yoo Seok Kim, Beom Seok Ko, Guiyun Shon, Yu Ra Lee, Hee Jeong Kim, Jong Han Yu, Jong Won Lee, Byung Ho Son, Sei Hyun Ahn*

Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea

Background/Purpose : Cytotoxic chemotherapy for breast cancer after surgery is one of the most important systemic therapy to reduce the recurrence rates and mortality rates. However, chemotherapy in elderly women with low risk, hormone receptor positive breast cancer is still inspires controversy. We report the outcomes in postmenopausal women with hormone receptor positive, HER-2 negative T2N0 breast cancer without adjuvant chemotherapy.

Methods : We analyzed retrospectively 207 postmenopausal women with hormone receptor positive, HER-2 negative T2N0 invasive breast cancer who underwent surgery at ASAN Medical Center from January 2000 to December 2008. The patients were devided two groups: endocrine therapy only (ET)(n=71) and adjuvant chemotherapy followed by endocrine therapy (CET) (n=136).

Results : ET group was older ($p<0.001$) and less received adjuvant radiotherapy ($p=0.003$) than CET group. There was more lymphovascular invasion in CET group than ET group ($p=0.001$). The number of removed axillary lymph node was greater in CET group than ET group ($p=0.019$). ET group showed a higher degree of progesterone receptor expression ($p=0.048$). In multivariate analysis, lymphovascular invasion was the only factor affecting risk of death and recurrence. There was no statistical significance in disease free survival rate, overall survival rate and disease-specific survival rate between two groups.

Conclusion : Some postmenopausal women with hormone receptor positive, HER-2 negative T2N0 breast cancer may avoid chemotherapy on the basis of biologic characteristics, comorbidity, social support, functional status, and patient's preferences. Tailored adjuvant therapy for early-stage breast cancer patients is an important goal.

PO04-26

IMPACT OF METFORMIN OF IN HORMONE RESPONSIVE, HER2 POSITIVE BREAST CANCER

Hyunwook Kwon[1], **Hee Jeong Kim**[2*], **Beom Seok Koh**[2], **Jong Han Yu**[2], **Byung Ho Son**[2], **Sei Hyun Ahn**[2]

[1] *College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*
[2] *Dept. of Breast Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*

Background/Purpose : Metformin use has recently been observed to decrease both breast cancer rate and mortality and a growing number of clinical intervention studies of metformin have been initiated. In our current study, the association between metformin use and survival outcomes was explored in diabetic and nondiabetic patients.

Methods : Data from the ASAN Medical Center Breast Cancer Database from 1997 to 2007 were analyzed. This study cohort comprised 6,591 non diabetic patients, 200 diabetic patients treated with metformin, and 179 diabetic patients that did not receive metformin

Results : Patients who were divided into three groups by diabetes status and metformin use were also divided into four subgroups by hormone receptor (HR) and HER2/*neu* status: Group1 (HR+ & HER2-), Group2 (HR+ & HER2+), Group3 (HR- & HER2+), and Group4 (HR- & HER2-). In Kaplan-Meier analysis, diabetic merformin users had a significantly increased survival duration compared with diabetic patients who received no metformin therapy (log-rank test, $p<0.001$) but no differences were seen compared with nondiabetics (log-rank test, $p=0.995$). In our subgroup analyses, only HR+ and HER2+ patients showed a disease-free survival benefit (log-rank test, $p=0.023$). After adjusting for age (< 50 years vs. ≥ 50 years), BMI BMI (<25 kg/m^2 vs. ≥25 kg/m^2), and stage, there were significant differences in disease recurrence of diabetic HR+ and HER2+ breast cancer patients between the nonmetformin and the metformin groups groups (HR=5.08, 95% CI=1.54-16.78, $p=0.008$) but not between the nondiabetics and metformin groups (HR=1.55, 95% CI=0.561-4.268, $p=0.399$)

Conclusion : Metformin may have a dramatic effect in diabetic HR+ & HER2+ patients in our study by simultaneously influencing multiple levels of cell signaling. Further randomized prospective clinical trials that evaluate the survival benefits of metformin will be necessary to prove our findings.

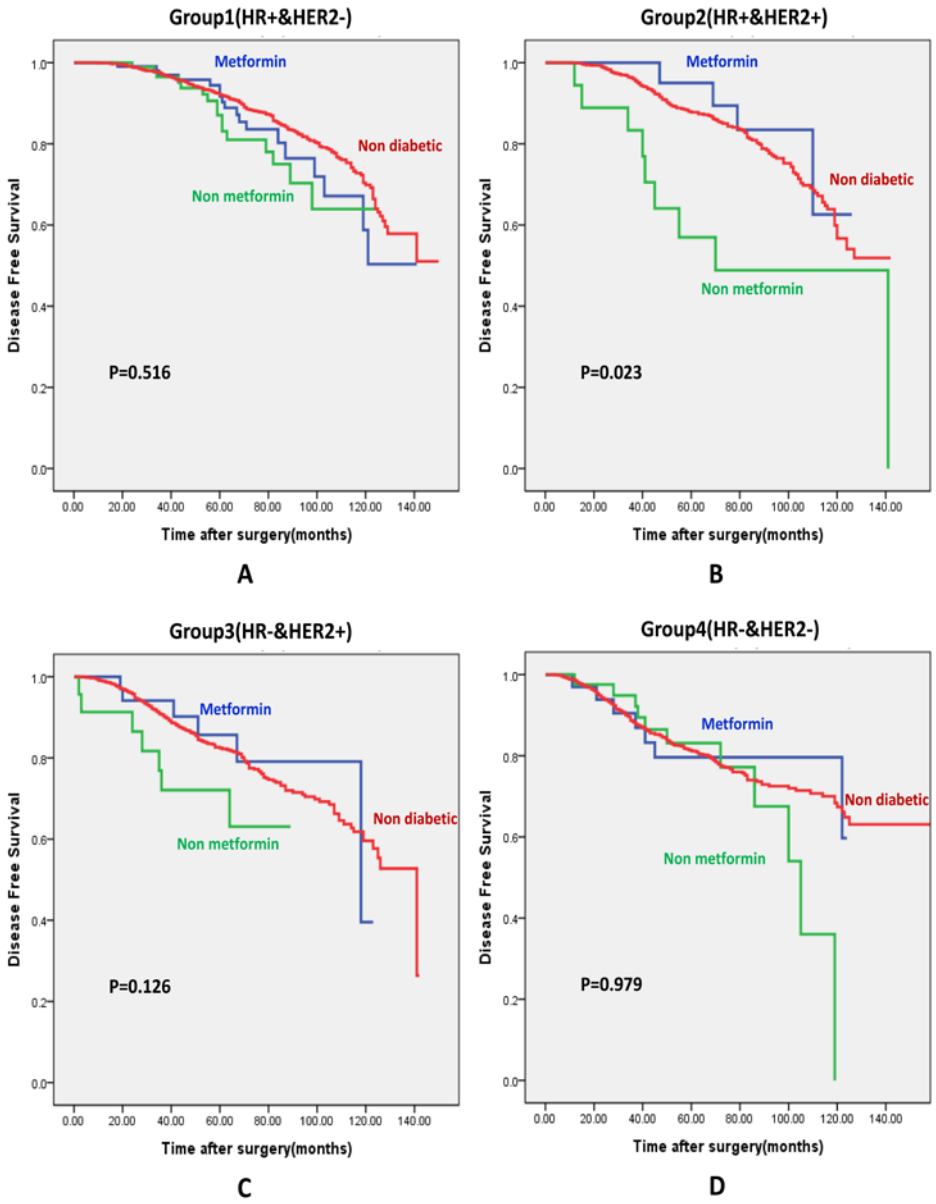
Group1(HR+&HER2-)
Metformin
Non diabetic
Non metformin
P=0.516
Disease Free Survival
Time after surgery(months)
A
Group2(HR+&HER2+)
Metformin
Non diabetic
Non metformin
P=0.023
Disease Free Survival
Time after surgery(months)
B
Group3(HR-&HER2+)
Metformin
Non diabetic
Non metformin
P=0.126
Disease Free Survival
Time after surgery(months)
C
Group4(HR-&HER2-)
Metformin
Non diabetic
Non metformin
P=0.979
Disease Free Survival
Time after surgery(months)
D

Figure 1

PO04-27

INTRAPLEURAL EXTRAVASATION OF ADRIAMYCIN AND CYCLOPHOSPHAMIDE

Jinyong Lee[1], **Sam Hi Kim**[1*], **Wun Won Kim**[2*], **Jeong Seon Lee**[1*]

[1] *Dept. of Breast Center & Surgery, Medical College, Inje Univ., Haeundae Hospital, Korea*
[2] *Dept. of Breast Center & Surgery, Medical College, Inje Univ., Korea*

Background/Purpose : The extravasation of vesicant cancer chemotherapeutic agents, especially anthracycline, remain one of the distressing complications, and can lead to extensive damage resulting from tissue necrosis at injury sites. In particular intrapleural or mediastinal extravasation of anthracycline via chemoport may cause horrible situation as life threatening complication.

Methods : We describe a 42-year old woman with breast cancer who received adjuvant chemotherapy after a breast conserving surgery. Due to misplacement of catheter tip of chemoport adriamycin and cyclophosphamide were administered intrapleurally. To minimize the detrimental sequella saline flushing of the thoracic cavity and systemic administration of steroid and 4th generation cephalosporine were performed. Besides of these empirical treatments 3 day-therapy schedule with dexrazoxane was added to prevent tissue damage and cardiac risk.

Results : The treatment with dexrazoxane could prevent tissue necrosis causing life threatening conditions successfully at accident of intrapleural extravasation of adriamycin and cyclophosphamide via chemoport. Thereafter she could finish adjuvat chemotherapy of 4 cycles of adriamycin and cyclophosphamide after complete recovery from extravasation accident.

Conclusion : Dexrazoxane proved to be an effective and well-tolerated acute treatment at intrapleural extravasation of adriamycin and cyclophosphamide. Dexrazoxane approved to prevent anthracycline cardiotoxicity, has now been authorized for intravenous treatment of anthracycline extravasation. However the assessment of dexrazoxane in anthracycline extravasation from a central line remains inadequate still now. We should optimize patient care by promptly recognizing and treating extravasation with dexrazoxane no longer than 6 hours after the extravasation accident. AS for preventive measure prior to starting chemotherapy Chest X-ray can ascertain proper catheter placement and may detect a fractured catheter or perforation of superior vena cava through saline infusion for overnight

PO04-28

EFFICIENCY OF METHYLENE BLUE NANOPARTICLES (nanoMB) AS LOCAL INJECTABLE AGENT FOR PHOTODYNAMIC THERAPY IN BREAST CANCER

Jin Hyang Jung[1], **Jin Gu Kang**[1], **Hyang Hee Choi**[1], **Seong Ook Hwang**[1], **Wan Wook Kim**[1], **Hoyong Park**[1*], **Se Hoon Kim**[2]

[1] *Dept. of Surgery, School of Medicine, Kyungpook National Univ., Korea*
[2] *Center for Theragnosis, Korea Institute of Science and Technology, Korea*

Background/Purpose : With advances in the early diagnosis of breast cancer and increased interest in life quality and cosmetic results, the rising demands for non-invasive or minimally invasive therapeutic methods for cancer have led to the accelerated development of medical technologies. One of them, photodynamic therapy (PDT), a non-invasive and alternative method for the treatment of cancer, is a light-activated treatment modality for breast cancer. Destruction of cancerous cells by PDT is achieved by a combination of photosensitizer and light of an appropriate wavelength for the photosensitizer. Methylene blue (MB) is a blue dye clinically being used and is known to show efficient photosensitizing activity with a very high yield of singlet oxygen generation (65%), where singlet oxygen is the actual therapeutic agent for PDT. However MB shows low cell uptake efficiency by itself and thus a low PDT efficacy. In this regard, we developed a nanoformulation of MB (nanoMB) to improve cancer cell uptake efficiency while keeping the high efficiency of singlet oxygen generation. NanoMB is composed of ternary components that are physically assembled in an aqueous milieu.

Methods : In this study, we investigated the cellular uptake of nanoMB and cancer cell apoptosis induced by nanoMB PDT in MDA-MB-231 human breast cancer cells in vitro and in vivo.

Results : In vitro, nanoMB was indeed avidly taken up by cancer cells (MDA-MB231), unlike free MB showing negligible cellular uptake. NanoMB formulation preserved the photosensitization activity of MB (singlet oxygen generation (SOG) quantum yield), without significant drop, under laser irradiation at 655 nm. Taken together, it was revealed from the in vitro microscopic observation that nanoMB can efficiently destroy live MDA-MB231 cells even under red lamp illumination. In the control group, cells were treated with free MB and did not show phototoxic influence under the same light. In the in vivo phototoxicity evaluation, the locally injected nanoMB was internalized into cancer cells. Upon annexin V treatment after laser irradiation at 655 nm, apoptosis of cancer cells was clearly observed from the spot where nanoMB and laser were applied together. The PDT-induced cell apoptosis was visualized in a simple mouse model by using fluorescently labeled annexinV that has high affinity toward apoptotic cells. Briefly, cancer cells were inoculated in muscle on opposite sides and nanoMB was applied to both the inoculation sites. After some time, only one side was laser-treated and fluorescent annexinV was injected to both. Only the dual-treated side (nanoMB + laser) showed retention of annexinV after 1 hour, indicating the occurrence of apoptosis by the PDT. Free MB and nanoMB were applied by subcutaneous injection around an early tumor tissue (not intratumoral injection). After 1 hour, free MB signals disappeared whereas nanoMB was retained at the tumor, implying that nanoMB penetrated into the tumor through the basement membrane. Laser irradiation was done one hour after sample injection for both free MB and nanoMB. This treatment (sample + laser) was

repeated seven times. According to the results, only nanoMB showed the tumor growth suppression effect, demonstrating the potential of nanoMB as a local injectable PDT agent.

Conclusion：In this study, nanoMB presented avid internalization into live cancer cells while keeping the high photosensitizing efficiency of MB. Consequently, highly efficient PDT of cancer cells was demonstrated in vitro and in vivo.

PO04-29

PROGNOSTIC OUTCOME OF SELECTIVE NECK DISSECTION IN ISOLATED IPSILATERAL SUPRACLAVICULAR LYMPH NODE METASTASIS (IISLNM) OF BREAST CANCER

Kwang Kuk Park, Song-I Yang, Dong-Won Ryu, Jeong-Hoon Kim, Chung-Han Lee*

Dept. of Surgery, College of Medicine, Kosin Univ., Korea

Background/Purpose : Clinically, ipsilateral supraclavicular lymph node metastasis in breast cancer can be classified into 2 manifestations: metachronous and synchronous. We performed this study to analyze the survival of breast cancer patients with isolated ipsilateral supraclavicular lymph node metastasis (IISLNM) and prognostic outcome of selective neck node dissection.

Methods : Forty-two patients who developed an IISLNM among 1363 primary breast cancer patients from January 2001 to December 2008 of at Kosin University Gospel Hospital. The clinical and biological features, the overall survival and disease free survival were compared for selective neck dissection and non-operation groups.

Results : Of the 1363 patients, 42 (3.1%) developed IISLNM during this period. All IISLNM positive patients had pathologic proof of IISLNM without evidence of any other distant spread by imaging findings. Among of them, Modified radical mastectomy was performed in 35 patients and breast conserving operation was performed in 7 patients. Selective neck node dissection was performed at 32 patients. The median patient age was 51.3 years. The median follow-up time from the initiation of therapy was 90.1 months. During the follow-up period, 22 patients died, and 5-year overall survival rate was 47.6%. Patients who received operation had a better 5-year overall survival rate than non-operation group (59.4% and 10.0%, p=0.004).

Conclusion : A surgical treatment should be established on IISLNM. As current include limited number of patients and a retrospective design, further studies more and long-term follow-up are required.

PO04-31

MANAGEMENT OF ACCESSORY BREAST TISSUES

Sung Ryul Lee

Dept. of Surgery, DAMSOYU Hospital, Korea

Background/Purpose : Approximately 0.4-6% of women have accessory breast. Although it doesn't involve special symptoms among most women, it can involve periodic physiologic and pathologic changes, just like normal breast tissue, under the influence of female hormones. Most indications for surgery are associated with pain in accessory breast or appearance issues.

Methods : Accessory breast excision was done on 364 patients with accessory breast from January in 2012 till June in 2013. Accessory breast excision including skin excision was done on 300 patients, while accessory breast excision with no skin excision was done on the other 64 patients. The surgery was performed by one surgeon.

Results : There were 164 married patients, 46 of whom had accessory breast symptoms with pain after giving birth, and 21 of those underwent surgery due to an appearance issue with no pain after giving birth. Among the 364 patients for surgery, 60 of them had accessory breast below normal breast, and 78 patients had their accessory nipple removed simultaneously. Inverted nipple correction was performed on 7 patients simultaneously, and reduction mammoplasty was done on 3 patients simultaneously. Thyroid lobectomy was performed on 2 patients diagnosed with thyroid cancer, and excision of benign tumor of over 1.0 cm was done on 16 patients. 8 patients who had liposuction at a plastic surgery clinic and 2 patients who had excision surgery experienced recurrence. As for complications, 7 patients experienced hematoma due to bleeding, and 7 patients had incision burns.

Conclusion : Most patients seeking accessory breast surgery have either pain or appearance related issues. In my hospital, 88 patients visited due to appearance issue with no pain, while 276 patients were struggling with pain. As for incision location, skin crease of axillary was incised about 2 cm, which was changed depending on the patient, and there was no drainage tube insertion after surgery. The number of seroma aspiration after surgery was 4 times on average (2-11 times). The average period of symptoms lasted 7 years and 2 months, and the average age of patients is 33 years (range, 17-57 years). The average weight of removed accessory breast is 70 g (range, 7-277 g), and the average volume of absorbed fat is 715 mL (range, 200-1,600 mL). In terms of treatment for accessory breast, I believe surgical excision is the best method to prevent recurrence. However, a liposuction along with excision surgery for treatment of the overall axillary can produce better cosmetic effects. Since 40% of married women are inflicted with accessory breast symptoms after pregnancy, I believe unmarried women with accessory mammary tissue should undergo excision surgery, even if she is not in pain. However, it would be necessary to minimize scars after axillary incision and reduce the absorption period as to serous fluid retention that occurs after a surgery.

PO05-01

WHEN SHOULD THE SCREENING PROGRAM FOR EARLY DIAGNOSIS OF BREAST CANCER BEGIN?

Ramazan Yildiz, Erkan Ozturk*, Yasar Subutay Peker, Zafer Kilbas, Mermet Fatih Can, Oner Mentes, Semih Gorgulu

Dept. of General Surgery, Gulhane Military Medical Academy, Turkey

Background/Purpose : Breast cancer peak decade is accepted as 6 decade. For this reason, breast cancer screening programs are usually adapted for patients elder than 50 years and screening programs adapted for patients younger than 50 years is still a discussion. In our country Turkey, there are studies emphasizing the decrease at the peak age of breast cancer. Our aim in this study is to discuss the beginning age of screening programs for breast cancer early diagnosis by exposing the age distribution of patients having the diagnosis of breast cancer at our clinic, in the consideration of literature data.

Methods : Demographic data of 623 patients, whom were operated at our clinic between 2000-2012 with the pre-diagnosis of breast cancer and had the histopathologic diagnosis afterwards were examined retrospectively.

Results : 623 breast cancer patients were operated in our clinic between 2000-2012 and were classified due to ages of diagnosis; 30-39 years: 91 (14.61%), 40-49 years: 181 (29.05%), 50-59 years: 164 (26.32%), 60-69 years: 104 (16.69%), 70-79 years: 58 (9.31%) and <30->79 years: 25 (4.01%) patients (Table 1). The mean of the patient's age were 52.45 years, and the most frequent age that the breast cancer was seen was 50 years with 26 patients. Most frequent second age that breast cancer was seen were 43-45-46-48 years with 23 patients and most frequent third ages were 44-51 years with 21 patients (Table 2). Most frequent 13 ages (as qualitative; respectively ages of 50-43-45-46-48-44-51-47-54-56-55-57-41), that breast cancer was seen, are the ages of 4th and 5th decades.

Conclusion : According to our results, patients having the diagnosis of breast cancer equal to or younger than 50 years old constitute approximately %44 of all breast cancer patients. This means that, almost one of 2 breast cancer patients are equal to or younger than 50 years. For this reason, we believe that the peak age of breast cancer should be debated. As a result, screening programs for early diagnosis of breast cancer should be adapted to younger women. This will increase the success of breast cancer screening programs and decrease the incidence of breast cancer.

PO05-02

THE VALUE OF SERIAL SERUM HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 (HER2) EXTRA-CELLULAR DOMAIN MEASUREMENT IN THE DETECTION OF RECURRENCE IN SURVEILLANCE OF HER2-POSITIVE BREAST CANCER PATIENTS AFTER PRIMARY THERAPY

June-Hyung Ha[1], Min-Ki Seong[1], Eun-Kyu Kim[1], Hyesil Seol[2], Jin-Kyung Lee[3], Woo Chul Noh[1], Jae Soo Koh[2], Hyun-Ah Kim[1]

[1] *Dept. of Surgery, Korea Cancer Center Hospital, Korea Institute of Radiological & Medical Sciences, Korea*
[2] *Dept. of Pathology, Korea Cancer Center Hospital, Korea Institute of Radiological & Medical Sciences, Korea*
[3] *Dept. of Laboratory Medicine, Korea Cancer Center Hospital, Korea Institute of Radiological & Medical Sciences, Korea*

Background/Purpose : Serum human epidermal growth factor receptor-2 extracellular domain (serum HER2) measurement is well established method to evaluate the response to HER2 targeted treatment in patients with metastatic HER2-positive breast cancer. However, little is known about value of serum HER2 in detecting disease relapses after curative operation in breast cancer patients. The purpose of this study is to evaluate the sensitivity of serum HER2, carcinoembryonic antigen (CEA) and carcinoma antigen 15-3 (CA15-3) in the detection of disease recurrence in post-operative breast cancer patients with primary HER2-positive tumor.

Methods : Serial serum levels of serum HER2, CEA and CA15-3 were evaluated in patients with primary invasive HER2-positive breast cancer who underwent curative operation between January 2008 and December 2010. After operation, the serum HER2 levels of the patients had been monitored every 6 months using the chemiluminescence immunoassay. The cut-off value for serum HER2 level was 15 ng/mL.

Results : A total of 264 patients were analyzed in this retrospective study. The median follow up period was 27.7 months. Twenty-four patients developed disease relapse during follow-up. At the time of disease recurrence, sensitivity of serum HER2, CEA and CA15-3 were 37.5%, 25.1% and 12.5%, respectively. The sensitivity was raised to 45.8% by combining all three tumour markers. In the subgroup of patients without liver disease, sensitivity of serum HER2, CEA and CA15-3 were 57.1%, 21.4% and 14.3%, respectively.

Conclusion : Serial serum HER2 measurements could be useful tumor marker to detect disease relapse in patients with HER2 positive breast cancer.

PO05-03

PREDICTOR FOR THE TRANSITION FROM DUCTAL CARCINOMA *IN SITU* (DCIS) TO INVASIVE BREAST CANCER AND THE VALUE OF MRI FOR EVALUATION

Keehoon Hyun, Woo Seok Byeon, Yong Lai Park, Chan Heun Park*

Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Breast and Thyroid Cancer Center, Kangbuk Samsung Hospital, Korea

Background/Purpose : To identify factors predictive of upstaging from diagnosed ductal carcinoma *in situ* (DCIS) to invasive cancer after surgical excision.

Methods : We evaluated the data of 60 patients with DCIS in minimally invasive biopsy specimens at Sungkyunkwan University Kangbuk Samsung between October 2009 and August 2012. Demographic, clinicopathological, radiological and histological variables were compared to identify predictors of invasive carcinoma in final pathology.

Results : The overall underestimated rate was 40.0% (24/60). Significant risk factors associated with the high level group in univariate analysis included ultrasound measured diameter, pathologic size and nuclear grade 3. In multivariate adjustment, ultrasound measured diameter (p=0.013), pathologic size (p=0.032) were independently associated with upstaging. We compared ultrasound with MRI by multivariate models and MRI measured diameters were not associated with upstaging (p=0.275).

Conclusion : Larger tumor size is the risk factor of upstaging to invasive cancer. Ultrasonographic size was associated with upstaging and MRI measured size was not.

PO05-04

RADIOLOGIC FEATURES ACCORDING TO THE MOLECULAR SUBTYPES IN DCIS OF THE BREAST

Yong Hwa Eom, Byung Joo Chae, Hee Yong Kwak, Young Ran Hong, Jae Beom Seo, Ja Seong Bae, So Hee Lee, Sang Seol Jung, Byung Joo Song*

Dept. of Surgery, College of Medicine, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Background/Purpose : The detection of ductal carcinoma *in situ* (DCIS) has increased significantly with the widespread use of screening mammography in asymptomatic women. Mammography is known the most valuable technique for the detection of DCIS. This study evaluated the morphological appearance of pure ductal carcinoma in situ of breast on mammography, sonography and MRI and assessed the correlation with molecular subtypes of DCIS.

Methods : The study involved 355 pure DCIS patients diagnosed between January 2004 and May 2013. All radiologic findings were reviewed in consensus according to the Breast Imaging Reporting and Data System. The histopathologic features of the lesions were obtained from medical records. Statistical comparisons were performed using the chi-square, Fisher's exact test.

Results : Mammography was performed in all 355 (100%) patients, sonograpy in 353 (99%), and MRI in 291 (82%). There were 288 (81%) patients with ER-positive and 67 (19%) patients with ER-negative disease. There were 92 (26%) patients with c-erbB2-positive and 263 (74%) patients with c-erbB2-negative disease. ER-negative DCIS was more likely to be high grade ($p<0.001$), high mastectomy rate (14.8% vs. 31.9%, $p=0.006$), high (≥14%) Ki-67 labeling index (LI) (45.9% vs. 54.1%, $p=0.001$), and associated with comedonecrosis (6.9% vs. 29.8%, $p=0.001$). But Multiple has no statistically significant difference in ER-negative DCIS and ER-positive DCIS ($p=0.636$). In imaging review, ER-negative DCIS was more likely to be visible in non-mass like type enhancement on MRI ($p=0.04$). No other statistically significant difference was in mammography and sonography features. C-erbB2-negative DCIS was more likely to be high mastectomy rate ($p=0.010$), low grade ($p<0.001$), high (≥14%) Ki-67 labeling index (LI) ($p<0.001$), and associated with comedonecrosis ($p<0.001$). But Multiple has no statistically significant difference in C-erbB2-negative and C-erbB2-positive DCIS ($p=0.569$). In imaging review, C-erbB2-negative DCIS was more likely to be detectable in mass like lesion than calcification on mammography and sonography ($p=0.030$ and $p=0.015$, respectively). There was no statistically difference in mass morphology and shape on mammography ($p=0.868$ and $p=0.251$, respectively). But Sonographic appearance of a round shape was more detectable in C-erbB2-negative DCIS. No other statistically significant difference was in MRI features.

Conclusion : In this study, ER-negative DCIS /ER-positive DCIS and C-erbB2-negative DCIS/C-erbB2-positive DCIS have different clinicopathologic and imaging characteristics on mammography, sonography, and MRI. Considering these findings, it may be helpful to detect DCIS and predict prognosis.

PO05-05

DEVELOPMENT AND VALIDATION OF MICROINVASION PREDICTION TOOL IN DCIS

Seongcheol Lee[1], **Youme Kim**[2], **Junwon Min**[1], **Myung-Chul Chang**[1*]

[1] *Dept. of Surgery, Dankook Univ. Hospital, Korea*
[2] *Dept. of Radiology, Dankook Univ. Hospital, Korea*

Background/Purpose : This study was to develop and validate nomogram to predict underestimation of ductal carcinoma *in situ* (DCIS) at breast core needle biopsy.

Methods : We developed a nomogram using previous reported meta-analysis study about DCIS underestimation. The factors related DCIS underestimation was palpability (OR=3.87), size more than 2 cm (OR=2.28), mammographic mass (OR=1.83), 14g automated vs. 11 g vacuum assisted (OR=1.85), histological high grade (OR=1.79). We developed web-based nomogram using a linear regression model with intercept calibration. To validate the nomogram, we used a retrospective data from January 2003 to September 2011. The accuracy of the nomogram was validated by comparing expected value and observed value assuming Poisson distribution and Hosmer-Lemeshow test. The discrimination was validated by ROC curve analysis.

Results : The developed nomogram was posted at the website
The developed nomogram was posted at the website. (http://user.dankook.ac.kr/~surgery/dcis/dcis-dku.htm). In the total sixty cases of DCIS cases diagnosed by core needle biopsy, twenty-nine cases (48.3%) were finally confirmed to have invasive component. The expected number of underestimation was not significantly different to the observed number according to the related factors. Also, the expected number was not significantly different to the observed number by the Hosmer-Lemeshow test. In the ROC curve analysis, the AUC was 0.823 (95%CI 0.720-0.926, $p<0.001$).

Conclusion : We developed a web-based nomogram to predict post-operative invasive component in pre-operative DCIS in core biopsy. This tool will be helpful about decision to do a sentinel node biopsy in first operation of DCIS in core biopsy.

PO05-06

THE ROLE OF PREOPERATIVE RADIOLOGIC EVALUATION FOR DETECTION OF AXILLARY LYMPH NODE METASTASIS

Chang Sik Shin, Jae Il Kim*

Dept. of Surgery, College of Medicine, Inje Univ., Ilsan Paik Hospital, Korea

Background/Purpose : The purpose of this study was to evaluate the availability of preoperative breast ultrasonography (US), magnetic resonance imaging (MRI), and positron emission tomography-computed tomography (PET-CT) for detection of axillary lymph node (LN) metastasis.

Methods : This study was designed as a retrospective, observational study at a single institution. The medical records of patients with breast cancer who underwent sentinel lymph node biopsy or axillary lymph node dissection after preoperative breast US, MRI and PET-CT between January 1, 2012 and May 31, 2013, were retrospectively reviewed. We analyzed positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of each radiologic modality.

Results : Of 69 patients with breast cancer underwent axillary surgery, 37 patients evaluated all radiologic modalities preoperatively. The mean age of patients was 50.7±11.4 years (range 33-80 years). 26 patients underwent planned sentinel lymph node biopsy (SLNB), and 11 patients underwent axillary lymph node dissection (ALND). 4 patients underwent SLNB needed ALND after frozen biopsy. The PPV was 46.2%, 46.7%, and 66.7%, and the NPV was 83.3%, 86.4%, and 80.6%, respectively. The sensitivity was 60.0%, 70.0%, and 40.0%, and specificity was 74.1%, 70.4%, and 92.6%, respectively.

Conclusion : PET-CT was the most predictive radiologic modality for detection of axillary LN metastasis considering higher PPV and specificity however, sensitivity was still lower. We suggest that a patient with negative finding of axillary LN on PET-CT and positive finding on breast US or MRI would undergo SNLB initially.

PO05-07

PREDICTION OF NEGATIVE SENTINEL NODE USING MULTIPLE IMAGING MODALITIES IN EARLY BREAST CANCER PATIENTS

Eun Jin Song[1], Ji Young You[1], Moo Hyun Lee[1], Youngmee Kwon[2], Kyoung Lan Ko[3], Kyung Hwan Shin[4], In Hae Park[5], Keun Seok Lee[5], Jungsil Ro[5], See Youn Lee[1], Han Sung Kang[1], Eun Sook Lee[1], So Youn Jung[1*]

[1] Dept. of Surgery, Center for Breast Cancer, National Cancer Center, Korea
[2] Dept. of Pathology, Center for Breast Cancer, National Cancer Center, Korea
[3] Dept. of Radiology, Center for Breast Cancer, National Cancer Center, Korea
[4] Dept. of Radio-Oncology, Center for Breast Cancer, National Cancer Center, Korea
[5] Dept. of Medical Oncology Center for Breast Cancer, National Cancer Center, Korea

Background/Purpose : The sentinel lymph node biopsy (SLNB) is a standard surgery of breast cancer. Recent SLNB is a tendency to shrink due to the development of adjuvant chemotherapy, radiotherapy, and hormonal therapy of breast cancer. The purpose of this study is to evaluate the nodal status using several preoperative imaging modalities and predict the negative value of the sentinel lymph node (SLN) in early breast cancer.

Methods : A total of 1008 patients with breast cancer, who underwent primary surgery from 2007 to 2012, were retrospectively analyzed. The clinicopathologic factors and imaging modalities including breast ultrasound (US), MRI, chest CT and PET were evaluated. We calculated predictive rates for node negativity in each imaging and developed the risk group with combination of tumor size and imaging modalities.

Results : Among total patients, 687 patients (68.2%) were SLN negative (68.2%), and 320 patients (31.8%) were node positive. Three hundred forty nine patients (34.6%) performed preoperative PET and 724 patients (71.8%) took the preoperative breast MRI. The patients with all US, MRI and PET results were total 275 patients. The scoring system using tumor size and the presence of axillary lymph node enlargement introduced and divided into 5 risk groups. The group of score 0 which is tumor size 1 cm or less and negative axillary lymph node enlargement in all US, MRI and PET were pathologically node positive rate of 7.7% ($p<0.001$). The patients who had the all results of preoperative chest CT, US, and MRI were 486. Among them, another scoring system using tumor size, chest CT, ultrasound, and MRI were tried. The patients in the tumor size less than 1cm and the negative results of three imaging modalities were 5 persons (10.2%, $p<0.001$). The pathologically positive value of lymph node showed trends to increase in relation to high score by both scoring systems.

Conclusion : The sentinel lymph node biopsy is still the standard surgical procedure of breast cancer management. As the development of imaging modalities, the clinically preoperative axillary nodal status of US, PET, chest CT, and MRI may help clinicians predict the negative value of sentinel lymph node. Furthermore, the multiple preoperative modalities will be able to offer clinicians the option to avoid unnecessary sentinel lymph node biopsy.

PO05-08

IS THERE DIFFERENT CORRELATION WITH PROGNOSTIC FACTORS BETWEEN "NON-MASS" AND "MASS" TYPED BREAST CANCERS?

Jungsun Lee[1*], **Sukjung Kim**[2], **Samhee Kim**[1], **Wun Won Kim**[1], **Jin Yong Lee**[1]

[1] *Dept. of Surgery, College of Medicine, Univ. of Inje, Haeundae Paik Hospital, Korea*
[2] *Dept. of Diagnostic Radiology, College of Medicine, Univ. of Inje, Haeundae Paik Hospital, Korea*

Background/Purpose : The MR breast imaging reporting and data system (BI-RADS) lexicon of the American College of Radiology (ACR) includes a new lesion category defined as non-mass like enhancement(NME). To investigate the association between non-mass typed solitary breast cancer (NME) and common clinical-pathological prognostic factors, compared with mass typed breast cancer.

Methods : After institutional review board approval, retrospective review was performed for 269 patients with primary breast cancer evaluated with gadolinium enhanced MRI, presenting from March 2010 to December 2012. Two radiologists assessed the image of each lesion for the morphologic enhancement type (mass enhancement or NME) and the distribution/internal enhancement for NME. Two pathologists evaluated the presence or absence of ductal carcinoma *in situ* (DCIS), number of metastatic lymph node, and expression status of estrogen receptor (ER)/progesterone receptor (PR)/HER-2/p53 tumor suppressor gene (p53)/Ki-67. Chi-square test and Spearman rank correlation were performed to explore the association of morphologic enhancement type with age, lesion size and the above pathological prognostic factors.

Results : Morphologic mass enhancement type (mean age: 52.2 years) was significantly correlated with older age than NME (mean age: 47.9 years, $p=0.01$). Mass typed breast cancers (1.9±1.1 cm) was larger than that of NME (1.8±1.3 cm), but not significantly ($p=0.07$). NME was also significantly correlated with presence of DCIS ($p=0.06$). Mass typed breast cancer was significantly correlated with invasive ductal carcinoma ($p<0.001$) and with Ki-67(+) ($p=0.013$), but NME with ductal carcinoma *in situ* ($p<0.001$) but not with lobular carcinoma ($p=0.24$). There was no significant correlation between morphological enhancement type and number of metastatic lymph node, ER/PR/HER2/p53 status. The clumped enhancement and segmental distribution was higher prevalence in NME. There was no correlation between enhancement distribution and clinicopathological prognostic factors.

Conclusion : NME may not necessarily have worse prognosis than the mass type, because of ductal carcinoma *in situ* and small size, although it may be occurred at younger age. Therefore, more data and large-scale studies are required to determine the clinical significance of NME with breast cancer.

PO05-09

CLINICOPATHOLOGIC SIGNIFICANCE OF FDG UPTAKE LEVEL USING PET CT IN PATIENTS WITH BREAST CANCER

Jina Lee, Young Hwa Kim, Jong Min Baek*, Ki Young Sung

Dept. of Surgery, The Catholic Univ. of Korea, Korea

Background/Purpose : The objective of this study is to investigate the clinical and biological significance of FDG uptake levels in breast cancer patients.

Methods : From May 2009 to February 2013, 228 women who underwent FDG PET/CT for staging of breast cancer were recruited retrospectively and 22 women were excluded whose primary tumors were not visualized with PET/CT. All of the breast cancers were newly biopsy-confirmed breast carcinoma and PET/CT were performed before definite breast cancer surgery or neoadjuvant/primary chemotherapy. Univariate analysis and multivariable analysis were used to test associations between FDG uptake levels in breast tumor and the clinical and molecular prognostic factors.

Results : Mean age of patients was 52.6 years. Mean SUV uptake levels was 6.32 and mean tumor size was 2.33 cm. PET/CT sensitivity for primary tumor detection was 90.4%. Axillary lymph node involvement was 30.1% and PET/CT sensitivity and specificity were 72.6% and 84.7% respectively. High SUV level was significantly correlated with large tumor size (>2cm, $p<0.001$), positive axillary lymph node metastasis ($p<0.001$), distant metastasis ($p=0.016$), higher TNM stage ($p<0.001$), higher histologic grade ($p<0.001$), higher nuclear grade ($p<0.001$), ER negativity ($p<0.001$), PR negativity ($p<0.001$), triple negativity ($p=0.006$), negative Bcl2 ($p=0.031$), positive CK-5/6 ($p=0.001$), positive EGFR ($p=0.005$), and positive Ki-67 ($p=0.003$). Multivariate analysis showed large tumor size (>2cm, $p=0.001$), positive axillary lymph node metastasis ($p=0.028$), and ER negativity ($p<0.001$) were significantly correlated with SUV in primary breast cancer.

Conclusion : High uptake FDG level in primary breast cancer was correlated with some poor prognostic factors and aggressive biologic markers such as ER negativity and Ki-67. The SUV using PET/CT might be predictive of some biologic markers and assist the therapeutic decision in the future.

PO05-10

F-18-FDG-PET/CT THYROID INCIDENTALOMA IN PRIMARY BREAST CANCER PATIENTS: A RETROSPECTIVE CASE-CONTROL STUDY

Sam Hee Kim[1], **Sung-Don Oh**[1], **Hyung-Kyung Sim**[2], **Wun Won Kim**[1], **Jin Yong Lee**[1], **Jungsun Lee**[1*]

[1] *Dept. of Surgery, College of Medicine, Univ. of Inje, Haeundae Paik Hospital, Korea*
[2] *Dept. of Nuclear Medicine, College of Medicine, Univ. of Inje, Haeundae Paik Hospital, Korea*

Background/Purpose : Thyroid incidentaloma diagnosed by 2-[18F]-fluorodeoxyglucose positron emission tomography (F-18-FDG PET/CT) is defined as a thyroid uptake incidentally and newly detected in a patient studied for nonthyroid purpose. The diagnostic and clinical significance of F-18-FDG PET/CT thyroid incidentalomas was not revealed during studies performed for an unrelated and nonthyroid disease, especially breast cancer. In this study, the prevalence of concurrent thyroid incidentaloma and its cancer risk rate were investigated by F-18- FDG PET/CT with primary breast cancer patients comparing general healthy women's population.

Methods : We retrospectively reviewed the medical records of patients with 489breast cancer patients and 286 healthy women who evaluated by 8-FDG PET/CT between March 2010 and December 2012.

Results : Data from the 18 F-FDG PET/CT study suggested the overall prevalence of thyroid incidentaloma was 17.6% (86/489) in breast cancer patients, and 4.2% (12/286) in healthy patients ($p<0.001$). Among 24 incidentaloma of breast cancer patients and 12 incidentaloma of healthy women with additional cyto-and histological diagnoses, papillary thyroid carcinoma was diagnosed in13 patients (54.1%)in breast cancer patients and 1patients (20%) in healthy women ($p=0.006$). Mean of SUVmax values was not significantly correlated with cytologic results (malignant: 7.89 vs. benign: 5.96, $p=0.63$). Of all primary breast cancer patients, patients with the older age ($p=0.07$), ER positive ($p=0.02$) have a tendency to have a thyroid incidentaloma. The common pathologic type of breast cancer with thyroid incidentaloma is specified ductal carcinoma ($p=0.031$) or lobular carcinoma ($p=0.07$) rather than invasive ductal carcinoma not otherwise specified (NOS).

Conclusion : FDG-PET thyroid incidentalomas are frequently detected by pre-treatment F-18- FDG PET/CT in patients with breast cancer comparing healthy women. The malignant rate of incidentaloma was slightly higher correlation with primary breast cancer compared with healthy women. Focal thyroid FDG-PET/CT incidentaloma with high SUV didn't warrant a pathological diagnostic procedure in this study. Therefore, more data and large-scale studies are required to determine the clinical significance of thyroid incidentaloma in patients with breast cancer.

PO05-11

PREDICTION OF PATIENT OUTCOME AFTER NEOADJUVANT CHEMOTHERAPY FOR TRIPLE NEGATIVE BREAST CANCER BY 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY

Sun Young Chae[1], Soyoung Jin[1], Jin-Hee Ahn[2], Sei Hyun Ahn[3], Byung Ho Son[3], Jong Won Lee[3], Kyung Hae Jung[2], Jungsu Oh[1], Sung-Bae Kim[2], Dae Hyuk Moon[1*]

[1] *Dept. of Nuclear Medicine, ASAN Medical Center, Korea*
[2] *Dept. of Oncology, ASAN Medical Center, Korea*
[3] *Dept. of Surgery, ASAN Medical Center, Korea*

Background/Purpose : 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) was shown to predict pathological complete response (pCR) after neoajuvant chemotherapy (NAC). We aimed to evaluate whether metabolic parameters of 18F-FDG PET can predict patient outcome in patients with triple negative breast cancer (TNBC) after NAC.

Methods : We retrospectively evaluated 95 female patients (mean age, 41. 4 years; range 23-68 years) with newly diagnosed with stage II or III triple negative breast cancer between January 2007 and December 2011. All patients were treated with NAC of an anthracycline- and/or taxane-based regimen followed by surgery. The ability of clinical and pathological parameters to predict patient outcome was assessed by multivariate analysis.

Results : Eighteen patients (19%) achieved a pCR. The maximal standardized uptake value (SUVmax) of the primary tumor and lymph nodes was higher in patients with pCR group than in those with non-pCR group ($p=0.012$) with an optimal cut-off value of 9.8 in predicting pCR. Median follow-up time was 26.6 mo (range, 10.4-77.7 mo). During this interval, 30 patients developed recurrent disease. Univariate analysis revealed that higher cT and cN; higher histologic grade; and a higher SUVmax were associated with disease-free survival (DFS) ($p<0.05$), whereas metabolic tumor volume and total lesion glycolysis were not ($p>0.05$ for each comparison). Multivariate analysis showed that cT ($p=0.008$; hazard ratio, 2.646) and SUVmax ($p=0.004$; hazard ratio, 0.304) were independent predictors of DFS.

Conclusion : SUVmax on baseline 18F-FDG PET/CT is an independent predictor of patient outcome after NAC for TNBC.

PO05-12

THE VALUE OF MAMMOGRAPHY, SONOGRAPHY AND MAGNETIC RESONANCE IMAGING FOR PREDICTION OF BREAST TUMOR SIZE: COMPARISON WITH PATHOLOGY MEASUREMENT

Inanc Guvenc[1*], **Sinan Akay**[1], **Ramazan Yildiz**[2], **Zafer Kilbas**[2], **Selami Ince**[1], **Mukerrem Safali**[3], **Mutlu Saglam**[1]

[1] *Dept. of Radiology, Gulhane Military Medical Academy, Turkey*
[2] *Dept. of Surgery, Gulhane Military Medical Academy, Turkey*
[3] *Dept. of Pathology, Gulhane Military Medical Academy, Turkey*

Background/Purpose : Exact preoperative breast cancer staging has important role determining of neoadjuvant chemotherapy candidates and surgical approach. The aim of this study was to evaluate sizing of primary breast cancer using mammography, sonography and MRI assess which imaging method most accurately compatible with the size of the pathological result.

Methods : Data from 62 patients with primary breast cancer were analysed in a retrospective study. The largest tumor diameter was measured with each imaging modality by two radiologists who had experience in radiological imaging of the breast. Pathologic size was used to determine the accuracy of imaging assessments. Statistical significance was accepted at the 95% confidence level ($P<0.05$). A commercially available software program was used for data processing and analysis.

Results : Tumor size was found to be significantly underestimated with sonography. The greatest difference between sonographic size and actual pathological tumor size was found with invasive lobular breast cancer. Tumor size by MRI was well correlated with pathology determined tumor size in both invasive ductal and invasive lobular breast cancer.

Conclusion : We conclude that MRI is the most accurate radiologic imaging method for assessment of the breast tumor size for determining exact preoperative staging.

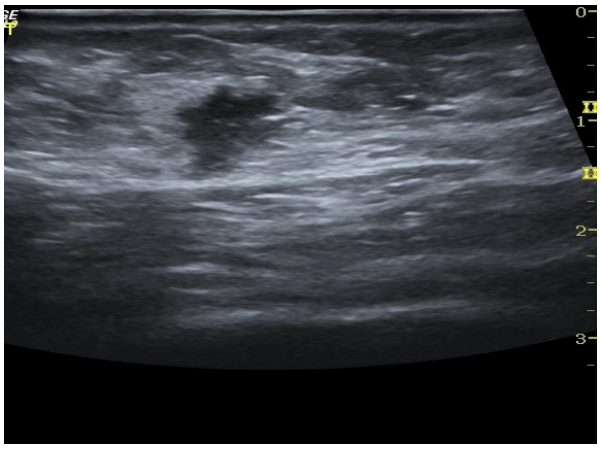

Figure 1

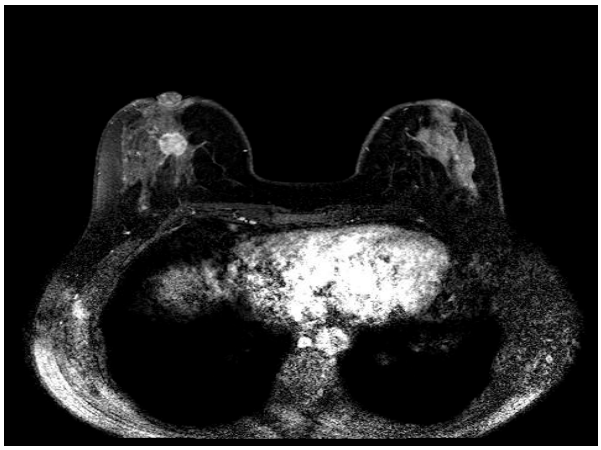

Figure 2

PO05-13

EVALUATION OF 18F FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY, MRI AND ULTRASOUND IN THE ASSESSMENT OF AXILLARY LYMPH NODE METASTASES IN PATIENTS WITH EARLY STAGE BREAST CANCER

Wooseok Byon, Keehoon Hyun, Yong Lai Park, Chan Heun Park*

Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Kangbuk Samsung Hospital, Korea

Background/Purpose : 18F Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) is a non-invasive imaging modality that can identify nodal metastases in women with primary breast cancer. The aim of this study was to compare the accuracy of FDG-PET with MRI and sonography scanning to determine axillary lymph node status in patients with breast cancer undergoing sentinel lymph node biopsy or axillary lymph node dissection.

Methods : Between January and December 2012, ninety-nine patients with breast cancer and clinically negative axillary nodes were evaluated. All patients underwent FDG-PET, MRI, ultrasound followed by sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND).

Results : Using axillary lymph node assessment as the gold standard, the sensitivity and specificity of FDG-PET were 51.4% (95% CI, 41.3%-65.6%) and 92.2% (95% CI, 82.7%-97.4%) respectively. The sensitivity and specificity of MRI and ultrasound were 57.1% (95% CI, 39.4%-73.7%), 67.2% (95% CI, 54.3%-78.4%) and 42.86% (95% CI, 26.3%-60.7%), 92.2% (95% CI, 82.7%-97.4%). Stratification according to hormone receptor status showed an increase in specificity when negative (FDG-PET: 42.3%-77.8%, MRI 50%-77.8%, ultrasound 34.6%-66.7%). Also, positive HER2 status was associated with an increase in specificity (FDG-PET: 42.9%-85.7%, MRI 50%-85.7%, ultrasound 35.7%-71.4%).

Conclusion : The sensitivity and specificity of FDG-PET compared with MRI and ultrasound was high. However, FDG-PET is not sufficiently accurate to appropriately identify lymph node metastases. This study suggests that FDG-PET scanning cannot replace histologic staging in early stage breast cancer, but might have a role in evaluating axillary lymph node status in hormone receptor negative or HER-2 overexpressing subtypes.

PO05-14

ROLE OF CONTRAST ULTRASOUND IN DIFFERENTIATION OF BENIGN & MALIGNANT FOCAL LESIONS OF THE BREASTS

Visnja Baksa Reynolds, Trishna Shimpi*

Dept. of Diagnostic Radiology, Khoo Teck Puat Hospital, Singapore

Background/Purpose : The aim of this study is to assess the efficacy of contrast-enhanced ultrasound (CEUS) scan to differentiate breast lesions, based on their enhancement pattern. The hypothesis is based on the phenomenon of neoangiogenesis in malignant lesions which produces difference in permeability and thereby the enhancement curves of malignant and benign lesions, in comparison to that of normal breast tissue.

Methods : CEUS examination of 28 breast lesions was performed using dedicated equipment (Toshiba Aplio XG). After injection of 2.4 ml of SonoVue (Bracco, Milan, Italy), the lesion was scanned using colour doppler and 3 dynamic sequences were recorded for 3 minutes, with each frame of 60 seconds (i.e., 0-60, 60- 120 and 120- 180 sec.). Two ROIs (region of interest) of similar size (6.2 mm^2) and at similar depth were placed in the lesion and in the normal breast tissue. Data was post-processed using Toshiba Contrast Harmonic Imaging Quantification (CHI-Q) software. The time-enhancement intensity curves (TEIC) for histopathologically malignant (category A) & benign (category B) lesions were obtained and compared with each other.

Results : All lesions were evaluated with biopsy and 17 invasive ductal carcinomas, 5 fibroadenomas, 2 fibro-cystic disease, 3 intraductal papillomatosis and 1 stromal fibrosis were diagnosed. TEIC for all malignant lesions (category A) were comparable to each other and showed lesser enhancement intensity (mean: -49.21) than the normal breast parenchyma (mean: -32.8). In the initial phase (0-60 sec), the malignant lesions revealed lower intensity (mean: -51.14), followed by slow, steady increase in intensity in the later phase of scanning, (mean: -47.8) at 180 sec. The benign lesions (category B), had a relatively wider range of intensities ranging from -47.6 to -56.9 with a mean value (-52.9), overlapping the intensity curve range of malignant lesions. The benign lesions also revealed lower enhancement intensity than the normal breast parenchyma.

Conclusion : CEUS of breast in our study had limited role in differentiation of sonographically indeterminate breast lesions due to overlap in their time enhancement intensity curves. Even though, CEUS curves of the benign and malignant lesions were quantitatively slightly different, a clear demarcation between the two could not be demonstrated. Previous studies discussed the dependency of the time intensity curve on the tissue depth. Relatively shallow position of the lesions in breast may influence the poor differentiation between malignant and benign lesions. A future study with different approach, like using virtual padding, may improve the efficacy of this emerging technique for better understanding of post contrast behavioural pattern of benign versus malignant breast lesions.

PO05-15

ADJUNCTIVE IMPRINT CYTOLOGY OF CORE NEEDLE BIOPSY SPECIMENS FOR BREAST CARCINOMA

Sae Ishihara, Shinichiro Kashiwagi*, Yuka Asano, Kento Kurata, Satoru Noda, Hidemi Kawajiri, Tsutomu Takashima, Naoyoshi Onoda, Kosei Hirakawa

Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan

Background/Purpose：Recently, therapies targeting the biological characteristics of individual cancers according to markers indicating underlying molecular biological mechanisms have become available. Core needle biopsy (CNB) is widely used, not only to diagnose, but also to determine therapeutic strategies, in patients with breast cancer. Although the diagnostic accuracy of CNB is acceptably high, false-negative results have occasionally been encountered.

Methods：The results of adjunctive imprint cytology (AIC) coinciding with CNB in 2,820 patients suspected to have breast cancer were retrospectively reviewed. The feasibility and clinical usefulness of AIC-assisted diagnosis were analyzed.

Results：Fourteen-hundred and sixty-four cases were diagnosed as not malignant using CNB alone. Forty-seven of 1464 cases were suspected to be malignant on a cytological review of AIC, and 42 were confirmed to be breast cancer on additional biopsies. The combination of CNB and AIC achieved a sensitivity of 100 % (1,398/1,398) and a specificity of 99.6 % (1,417/1,422). Small lesions and large noninvasive or scirrhous-type carcinomas were the common features of the CNB-negative/AIC-positive cases.

Conclusion：Adjunctive imprint cytodiagnosis is a simple and easy procedure that assists the pathological diagnosis of breast cancer using CNB and therefore serves as a possible novel standard application.

PO05-16

THE CLINICAL STUDY OF PAPILLARY LESIONS OF THE BREAST THAT ARE DIAGNOSED BY VACUUM ASSISTED BREAST BIOPSY

Hai-Lin Park[1*], **Ji-Sun Hong**[2]

[1] *Dept. of Surgery, College of Medicine, CHA Univ., Kangnam CHA Hospital, Korea*
[2] *Dept. of Breast and Thyroid Surgery, Kangnam CHA Hospital, Korea*

Background/Purpose : Our aim was to evaluate the clinical characteristics of the papillary lesions of the breast diagnosed by vacuum assisted breast biopsy (VABB) and to identify the difference benign from malignant papillary lesions.

Methods : From January 2007 to December 2012, a total of 223 ultrasound-guided Mammotome excision were performed and proved to be papillary lesions. Sonographic features were retrospectively reviewed according to the BI-RADS lexicon. Morphology, not part of BI-RADS, was assessed according to the relationship between the mass and the duct as four types; type I, intraluminal mass; type II, extraductal mass; type III, purely solid mass; type IV, mixed. Type I was subdivided into intraductal type (Ia), intracystic type (Ib), and solid type with an anechoic rim (Ic).

Results : Pathologically, 202 lesions were benign, showed intraductal papillomas (n=195, 87.5%) and papillomatosis (n=7, 3.1%). The remaining 21 lesions were malignant including atypical papilloma (n=7, 3.1 %), intraductal papillary carcinoma (n=11, 4.9%) and invasive papillary carcinoma (n=3, 1.3%). 116 lesions (52%) were classified as Type III purely solid mass, 75 lesions (33.6%) were Type I intraluminal mass, 22 lesions were Type II extraductal mass and 10 lesions were Type IV mixed type according to the ultrasound findings. There was no significant difference in the benign, malignant lesions with age, bilaterality or distance from nipple. But, malignant papillary lesions had a larger mean lesion size (1.64±1.01 cm) compared with the benign lesions (1.09±0.65 cm) significantly (p=0.005).

Conclusion : Only half of the papillary lesions have the sonographic findings suggestive of intraductal origin (Type I, II, IV) and the majority of the lesions (52%) displayed a solid appearance (Type III). There was significant difference in the benign, malignant papillary lesions of the breast with size.

PO05-17

CLINICAL AND HISTOPATHOLOGIC T STAGE DIFFERENCES IN BREAST CANCER DIAGNOSED WITH VACUUM-ASSISTED BREAST BIOPSY

Hai-Lin Park[1*], **Ji-Sun Hong**[2]

[1] *Dept. of Surgery, Kangnam CHA Hospital, Korea*
[2] *Dept. of Breast and Thyroid Surgery, Kangnam CHA Hospital, Korea*

Background/Purpose : This study aimed to determine the difference between clinical T stage based on preoperative ultrasound and histopathologic T stage after surgery in vacuum-assisted breast biopsy (VABB)-diagnosed breast cancer.

Methods : Tumor sizes measured ultrasonographically and histologically were retrospectively calculated and analyzed using paired t-tests in 209 patients diagnosed with breast cancer using VABB. Patients were classified two groups as BI-RADS 4a or below (complete resection by VABB) and BI-RADS 4b or above (incisional biopsy by VABB).

Results : Histopathologic tumor size was smaller than the size on ultrasonogram in 92.3% of pT1a, 75.5% of pT1b, 44.2% of pT1c, 47.7% of pT2, and 0% of pT3 cases. Further, histopathologic tumor size was smaller than the USG size in 62.8% of cases at BI-RADS 3-4a and in 53.7% of cases at BI-RADS 4b-5.

Conclusion : The smaller the primary tumor at the time of diagnosis by VABB, the higher the likelihood of pathologic underestimation on postoperative histopathologic assessment compared to preoperative USG.

PO05-18

A SIMPLE METHOD FOR RELATIVE ASSESSMENT OF SOUND PROPAGATION VELOCITY IN BREAST TUMOR

Dong Won Ryu*, Chung Han Lee, Youn Suk Kim, Kwang Guk Park

Dept. of Breast Surgery, Kosin Univ. Gospel Hospital, Korea

Background/Purpose : Previous studies using ultrasound CT or clinical amplitude/velocity reconstruction imaging ultrasound may indicate that cancers differ from normal breast tissue by increased sound velocity. However, only limited experience with direct measurements of sound velocity exists. This study aimed to investigate the sound propagation velocity in breast tumors relative to the velocity in adjacent tissue.

Methods : One hundred patients with palpable breast tumors were studied. One hundred patients (50 benign tumors, 50 malignant tumors) were analyzed. The scanning plane was aligned so that it transected the tumor and depicted the front of a rib or the pleura-lung interface behind the tumor. This contour was evaluated for distortion, and the height of the distortion and the height of the tumor were used to calculate the relative sound propagation velocity.

Results : A posterior reference line was revealed behind 98 of 100 tumors. Of these 98 tumors, an elevation was seen behind 98 tumors, and no distortion was seen behind 2 tumors. A depression was never observed. The median relative sound propagation velocity of 1.07 that was calculated in 48 carcinomas (range, 1.00-1.14) was insignificantly higher (p=0.179) than the median relative sound propagation velocity of 1.04 obtained in 50 fibroadenomas (range, 1.00-1.15).

Conclusion : Although assessment of relative sound propagation velocity in breast tumors was successful, the relative velocities differed only insignificantly between benign and malignant lesions.

PO06-01

TISSUE ARRAY CONFIRMS PKCα EXPRESSION CORRELATED WITH THE EXPRESSION OF ELK-1 AND MZF-1 IN INVASION AND METASTASIS OF BREAST CANCER

Yung Wei Chiu[1*], Chia-Herng Yue[2], Li-Hwa Lu[1], Jai-Nien Tung[2], Ho Lin[3], Jer-Yuh Liu[4*], Te-Jen Lai[5]

[1] *Dept. of Emergency, Tungs' Taichung MetroHarbor Hospital, Taiwan*
[2] *Dept. of Surgery, Tungs' Taichung MetroHarbor Hospital, Taiwan*
[3] *Dept. of Life Science, National Chung Hsing Univ., Taiwan*
[4] *Graduate Institute of Cancer Biology, China Medical Univ., Taiwan*
[5] *Institute of Medicine, College of Medicine, Chung Shan Medical Univ., Taiwan*

Background/Purpose : Our recent study has shown that elevated expression of PKCα in breast cancer cell lines may be correlated with the potential of cell migration and invasion, and the transcription factors Myeloid Zinc Finger-1 (MZF-1) and Ets-like-protein 1 (Elk-1) are related to protein kinase C alpha (PKCα) expression. However, little is known about the correlation of PKCα and these transcription factors in surgical specimens of human breast cancer.

Methods : Tissue microarray blocks of 208 breast cancer lesions were evaluated by immunohistochemistry for the expression of the selected transcription factors and PKCα. Aberrant expression was correlated statistically with tumor characteristics and disease outcome.

Results : Of the 208 breast cancer lesions, the rate of PKCα, Elk-1 and MZF-1 overexpression were high. The correlation of PKCα and these transcription factors in metastastic breast cancer was 63.9%.

Conclusion : Our results support that breast cancer appears to be associated with overexpression of PKCα, Elk-1 and MZF-1. Since metastasis of breast cancer overexpresses PKCα and upstream transcription factors, this may be a candidate for therapeutic target.

PO06-02

AN ANALYSIS OF DIFFERENT FACTORS RELATED TO EARLY AND LATE RECURRENCE IN PRIMARY BREAST CANCER

Reiki Nishimura[1], **Tomofumi Osako**[1], **Yasuyuki Nishiyama**[1], **Rumiko Tashima**[2], **Masahiro Nakano**[1], **Mamiko Fujisue**[1], **Yasuo Toyozumi**[3], **Nobuyuki Arima**[3]

[1] *Dept. of Breast & Endocrine Surgery, Kumamoto City Hospital, Japan*
[2] *Dept. of Surgery, Kumamoto City Hospital, Japan*
[3] *Dept. of Pathology, Kumamoto City Hospital, Japan*

Background/Purpose : Breast cancer is a heterogeneous disease and is associated with a relatively favorable prognosis. Prognostic factors examined to date are related to early recurrence while those related to late recurrence and their countermeasures remain unclear. Therefore, we examined the factors related to late recurrence, ≥10 years after initial treatment, and compared them with the factors related to early (< 5 years) recurrence.

Methods : From 1980 to May 2013, 4949 patients who underwent primary treatment, including operation, estrogen receptor (ER) and progesterone receptors (PgR) measurement, were enrolled in this study. There were two patient groups; those for analysis of factors for 5-year disease-free survival (DFS) and those (1,424 patients) without any recurrence at 10 years but who continued follow-up examinations. Recurrence occurred in 575 and 125 patients within 5 and 10 years, respectively, and occurred in 57 patients from ≥ 10 years. The items examined were tumor size, lymph node status, and the following biological markers; ER, PgR, Ki-67 values, p53 and human epidermal growth factor receptor 2 (HER2) expressions.

Results : The overall 10-year cumulative DFS rate was 79.9%, and the recurrence rate at ≥10 years was 6.1% (some cases had recurrence after 20 years). A multivariate analysis revealed that the factors related to late recurrence were positive nodes and PgR positive. This result differed from that for early recurrence, where the DFS rate was low in patients who had ER/PgR negative, a high Ki-67 index value, and HER2 positive and p53 overexpression.

Conclusion : The PgR positivity and lymph node metastasis significantly correlated with late recurrence (≥10 years after primary treatment) in primary breast cancer. Therefore, it is important to evaluate the treatment period and treatment regimen for hormone-sensitive (ER and/or PgR positive) patients.

PO06-03

SIGNIFICANCE OF C-KIT EXPRESSION IN BASAL-LIKE BREAST CANCER

Shinichiro Kashiwagi*, Masakazu Yashiro, Sae Ishihara, Yuka Asano, Kento Kurata, Naoki Aomatsu, Satoru Noda, Hidemi Kawajiri, Tsutomu Takashima, Naoyoshi Onoda, Kosei Hirakawa

Dept. of Surgical Oncology, Graduate School of Medicine, Osaka City Univ., Japan

Background/Purpose : As patients with basal-like breast cancer (BLBC) have a poor prognosis and have no specifically tailored therapy, molecular biological characterization of BLBC is necessary. c-Kit is a transmembrane receptor tyrosine kinase known to play important roles in various solid cancers. Therefore, this study classified BLBCs from patients with breast carcinoma, and addressed the significance of c-Kit expression in these tumours.

Methods : Primary breast tumours were stained with antibodies against oestrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 (HER2), epidermal growth factor receptor (EGFR), cytokeratin 5/6 and c-Kit. The association between c-Kit, BLBC and survival was analyzed.

Results : A total of 667 patients with breast cancer were followed up for a median of 39 (range 6-72) months. Some 190 tumours (28.5%) were classified as triple-negative for breast cancer (negative for oestrogen receptor, progesterone receptor and HER2), and 149 (78.4%) had characteristics of BLBC (positive for CK5/6 and/or EGFR). c-Kit expression was detected in 111 (16.6%) of 667 tumours. c-Kit-positive tumours were more commonly found among patients with BLBC (42 of 149 [28.2%], $p<0.001$) and in patients with nodal metastasis (47 of 216 [21.8%], $p=0.014$) than in those without. In patients with BLBC, the prognosis was significantly worse in those with c-Kit expression ($p<0.001$). Multivariable logistic regression analysis revealed c-Kit as an independent negative prognostic factor for cancer-specific survival in patients with BLBC (hazard ratio 2.29, 95% CI 1.11-4.72).

Conclusion : c-Kit might be a prognostic marker and possible molecular target for therapy in patients with BLBC.

PO06-04

CLINICOPATHOLOGIC REVIEWS OF METAPLASTIC CARCINOMA OF BREAST FROM SEVEN KOREAN BREAST CANCER CENTERES

Yu Mi Ra[1], Dae Sung Yoon[1*], Sung Hoo Jung[2], Jung Han Yoon[3], Eil Sung Chang[4], Je Ryong Kim[4], Myung-Chul Chang[5], Sung Yong Kim[6], Kwang Man Lee[7]

[1] *Dept. of Surgery, Konyang Univ. Hospital, Korea*
[2] *Dept. of Surgery, Medical School, Chonbuk National Univ., Korea*
[3] *Dept. of Surgery, Chonnam National Univ. Hwasun Hospital, Korea*
[4] *Dept. of Surgery, College of Medicine, Chungnam National Univ., Korea*
[5] *Dept. of Surgery, College of Medicine, Dankook Univ., Korea*
[6] *Dept. of Surgery, Soonchunhyang Univ. Hospital, Korea*
[7] *Dept. of Surgery, School of Medicine, Wonkwang Univ., Korea*

Background/Purpose : Metastatic breast cancer (MBC) is a rare subtype , accounting for < 1% of all breast cancer, and has a poor prognosis than most other breast cancers. We analyzed 54 patients of metaplastic carcinoma from seven Korean breast cancer centers.

Methods : The clinicopathological characteristics and clinical outcomes were retrospectively reviewed. 9993 patients was performed operation with breast cancer in seven hospitals since January, 2000.

Results : Metaplastic carcinoma was 0.5% of breast cancers. Mean duration of follow up was 48.31 mo (1-183 mo). Mean age of patients was 50.65 yr (32-75 yr). BMI was 23.26 (10.8-36). 16 patients (29.6%) were performed breast conserving surgery and 13 patients (24.1%) were performed sentinel lymph node biopsy. The patients presented with a large tumor size (≥T2, 68.5%), axillary lymph node metastasis for 27.8%, and distant metastasis at first diagnosis for 5.6%. Estrogen receptor and progesterone receptor positivity was showed in 18.5% and 22.1%. Triple negative breast cancer was in 53.7%. 39 patients(72.2%) had received chemotherapy with various chemotherapeutic regimens; 12 AT (doxorubicin, docetaxel), 7 AC (doxorubicin, cyclophosphamide), 6 FAC (5-fluorouracil, doxorubicin, cyclophosphamide), 5 CMF (cyclophosphamide, methotrexate, 5-fluorouracil) and 10 others. 14 patients (25.9%) had recurrences detected at a mean 12.3 months after surgery. 5 patients had local recurrence and 9 patients had distant metastasis; lung metastasis for 5, brain, liver and cervical lymph node metastasis. 7 patients(12.7%) was expired at a mean 16.7 months after surgery. 5-year survival was 83.3%.

Conclusion : Metaplastic breast cancer is rare, but has distinct aggressive features. It is diagnosed with large tumor and advanced stage, but less lymph node metastasis. It also has early recurrence and more distant metastasis for recurrence patterns. The patients with recurrence tend to have more advanced stage at diagnosis than those without recurrence, but there are no differences in other clinicopathologic characteristics between two groups. Further studies such as biochemical markers for predicted recurrence or worse prognosis are necessary. Because of their rarity and heterogeneity, there is no standard therapy. Therefore, we should consider metaplastic cancer as distinct subtype and approach with tailored methods.

PO06-05

PROGNOSTIC SIGNIFICANCE OF ESTROGEN RECEPTOR β IN BREAST CANCER

Tae Hyun Kim*, Jae Hyun Kang, Kyung Do Byun, Ah Rheo Yun

Dept. of Surgery, Inje Univ., Busan Paik Hospital, Korea

Background/Purpose : Estrogen is associated with increased risk for development and progression of breast cancer. Estrogen receptor α (ERα) and Estrogen receptor β (ERβ) have revealed as site of direct action of estrogen on nuclear DNA. ERα and ERβ can have opposite actions due to the difference in ligand binding between both. ERα is a well-known prognostic marker and a predictive marker for the response to hormonal therapy. However, the role of ERβ is less well understood. Prognostic significance of two estrogen receptor would be complex according to their different affinity to same ligand and their ratio of presence. The aim of this study is elucidate the role as prognostic factor of ERβ in breast cancer

Methods : Tissue microarrays were performed for six blocks containing 89 cases of invasive ductal carcinomas diagnosed between 1999 and 2001. Patients with less than stage IIIB were 73. Recurrent rate and survival rate were analyzed according to ERα and ERβ expression status. The relationships between ERα and ERβ expression and age, tumor size, lymph node status, stage, histological grade, expression of ER, progesterone receptor, human epidermal growth factor receptor 2 (HER2), epidermal growth factor and p53 were analyzed.

Results : Sixty six patients showed positive for ERβ and 68.2% of 10 year survival rate (YSR). On the contrary, 7 patients with negative for ERβ showed 42.9% of 10 YSR. 10YSR was 67.6% in patients with lower expression of ERα than ERβ (1 ≤ ERα/ERβ ratio) and 61.9% in patients with higher ERα than ERβ (1 > ERα/ERβ ratio). The patients with ERα positive/ERβ positive looked to have increased disease-free survival (DFS) and overall survival (OS) than those with ERα positive/ERβ negative, ERα negative/ERβ positive, and ERα negative/ ERβ negative. However it was not statistically significant. DFS and OS of the ERβ positive patients increased more than those ERβ negative patients in the ERα positive subgroup, the subgroup treated with tamoxifen, and the triple negative subgroup, but these increases were not statistically significant.

Conclusion : ERβ expression would be better prognostic sign in breast cancer. Further studies are needed to assess the role of ERβ expression in breast cancer.

PO06-06

HAZARD OF RECURRENCE AFTER BREAST OPERATION ACCORDING TO HORMONE RECEPTOR STATUS AND AGE

Seung Pil Jung[1], **Se Kyung Lee**[2], **Sangmin Kim**[2], **Soo Youn Bae**[2], **Jiyoung Kim**[2], **Minkuk Kim**[2], **Won Ho Kil**[2], **Seok Jin Nam**[2], **Jeoung Won Bae**[1], **Jeong Eon Lee**[2*]

[1] *Divison of Breast and Endocrine Surgery, Dept. of Surgery, College of Medicine, Korea Univ. Hospital, Korea*
[2] *Divison of Breast and Endocrine Surgery, Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : Breast cancer can recur many years after treatment. Age and hormone receptor status have been reported to be related with recurrences in breast cancer. Most studies have focused on disease free survival and survival curves. We estimated hazard rates for recurrence to evaluate the risk of recurrence at a given time and how to recurrence changes over time according to hormone receptor status and patient age.

Methods : We retrospectively reviewed the medical records of 6308 patients with stage T1-3 breast cancer who received breast cancer operation from August 1995 to December 2010. We excluded women treated with trastuzumab to avoid the bias from different treatment. Recurrence was defined as not only locoregional but also any distant recurrences. Hazard rates were estimated by using Proc Lifetest in SAS through the Kaplan-Meier method. Patients were grouped according to ER status; ER(+) (n=4,589), ER(-) (n=1,719) and age; less than 39 year (n=1,192), 40-59 years (n=4,250), more than 60 years (n=866).

Results : Median follow up period was 60 months. Estimated 5-year and 10-year recurrence rate calculated by using the Kaplan-Meier method were 11.2% and 19.5% in overall cohort. Estimated 5-year and 10-year recurrence rate were 10.6% and 19.6% in ER(+) patients, and 16.6% and 18.4% in ER(-) patients. For the age group, estimated 5-year and 10-year recurrence rate were 18.5% and 28.9% in <40 year group, 10.2% and 16.3% in 40-59 year group and 15.3% and 22.3% in >60 year group. Hazard of recurrence (HR) was highest in 2-3 years after surgery in overall cohort. ER(-) patients showed steep pattern of HR, while ER(+) patient showed steady pattern of HR. Five years after surgery, HR was higher in ER(+) patients than ER(-) patients. Younger patients showed higher HR than older patients regardless of ER status and stage.

Conclusion : Our study suggest that ER(-) patients showed high recurrence rate in early post-operative stage, however, in late post-operative stage, ER(-) patient showed lower recurrence rate than ER(+) patient. In young patient, the effect of ER status on recurrence might be reduced than older patient. Young patients should be carefully observed because of high and long standing hazard of recurrence especially in ER(+) patients.

PO06-07

CLINICOPATHOLOGICAL FEATURES AND PATIENT SURVIVAL IN BREAST CANCER PATIENTS WITH EARLY AND LATE TUMOR RECURRENCE AFTER ADJUVANT CHEMOTHERAPY

Young Mi Yun[1], Gui Yun Son[1], Sei Hyun Ahn[1], Jong Won Lee[1], Hee Jeong Kim[1], Jong Han Yu[1], Beom Seok Ko[1], Yu Ra Lee[1], Heeseung Park[1], Sung Bae Kim[2], Gyung Yub Gong[3], Byung Ho Son[1*]

[1] *Dept. of Surgery, Univ. of Ulsan, ASAN Medical Center, Korea*
[2] *Dept. of Oncology, Univ. of Ulsan, ASAN Medical Center, Korea*
[3] *Dept. of Pathology, Univ. of Ulsan, ASAN Medical Center, Korea*

Background/Purpose : The purpose of this study is to compare the clinicopathological features and survival in breast cancer patients with early and late recurrence after adjuvant chemotherapy.

Methods : A total of 1,089 recurrent breast cancer patients who registered in the ASAN Medical Center Breast Cancer Registry between July 1989 and February 2010, were divided into three groups, i.e. an early recurrent (within two years) and two, late recurrent groups (2-5 years and after five years). Conventional prognostic factors including the tumor stage, nodal status, histologic grade, nuclear grade, hormone receptor, HER2, and tumor subtype were compared in order to identify whether any factor would show a significant difference in these recurrent patient groups. The univariate survival distributions were estimated using the method of Kaplan-Meier and they were compared using the log rank test. The potential prognostic factors were analyzed using multivariate analysis with Cox proportional hazard model.

Results : The tumor stage ($p<0.0001$), size ($p=0.0015$), number of lymph node metastases ($p=0.0007$), histologic grade ($p<0.0001$), nuclear grade ($p<0.0001$), estrogen receptor ($p<0.0001$), progesterone receptor ($p<0.0001$), and tumor subtype ($p<0.0001$) differed significantly among the early and late recurrent groups. The median patient survival time after recurrence in the early recurrence group (18 months) was significantly shorter than that seen in the late recurrence groups (28 months in the group 2-5 years and 49 months in the group after 5 years). The multivariate analysis showed that early recurrence (HR=2.54, 95% CI=1.50-4.32, $p=0.0005$), advanced stage (II, HR=2.10, 95% CI=1.43-3.07, $p=0.0002$; III, HR=2.54, 95% CI=1.72-3.74, $p<0.0002$), high histologic grade (HR=1.45, 95% CI=1.16-1.81, $p=0.001$), positive estrogen receptor (HR=0.60, 95% CI=0.46-0.77, $p<0.0001$), and the triple-negative subtype (HR=2.05, 95% CI=1.50-2.80, $p<0.0001$) were independent prognostic factors for overall patient survival following recurrence.

Conclusion : This study showed that aggressive clinicopathologic features and the triple-negative subtype were associated with the early recurrence of breast cancer after chemotherapy. The survival time after recurrence in the early recurrence patients was significantly shorter than those of the late recurrence patients.

PO06-08

THE PROGNOSTIC VALUE OF KI-67 LABELING INDEX IN PRIMARY OPERABLE BREAST CANCER

Uiju Cho[1], **Ahwon Lee**[1*], **Byung Joo Chae**[2], **Byung Joo Song**[2], **Sang Seol Jung**[2]

[1] *Dept. of Hospital Pathology, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*
[2] *Dept. of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*

Background/Purpose : Tumor proliferation is considered have prognostic importance in breast cancer. However, immunohistochemical staining of Ki-67 protein, which is a routinely evaluable proliferation marker, have been reported as a prognostic factor with variable cut-off values to distinguish KI-67 high from low.

Methods : We immunohistochemically assayed proliferation activity of operable BC in 589 consecutive patient who underwent surgical resection between January 2003 and January 2007. Ki-67 immunostaining was performed on 2.0 mm core tissue microarray (TMA) and then the labeling index (LI) was manually counted using image processing program (Adobe photoshop). We also compared manual count of Ki-67 LI with whole section eyeballing Ki-67 LI acquired from pathologic report.

Results : Mean ages of the patients are 50 years old and mean follow up period was 76 months. Univariate survival analysis showed statistically significant difference in long term breast cancer associated death in following factors; histologic grade, lymph node metastasis stage, esterogen receptor status, progesterone receptor status and HER2 status ($p=0.005$, $p<0.001$, $p=0.003$, $p=0.21$ and $p=0.027$, respectively). Cut-off values (10%, 14% and 20%) were chosen with the review of literature before statistical analysis. Manual and eyeballing Ki-67 evaluation are statistically well correlated (Pearson correlation=0.683, $p<0.001$). Manual and eyeballing Ki-67 LI agreement rate was highest in cut-off value of 20% (Kappa coefficient=0.340, 0.447, and 0.716 with cut-off value of 10%, 14% and 20%, respectively). With the cut-off values of 14% and 20%, High Ki-67 LI was associated with poor breast cancer specific survival ($p=0.028$ and $p=0.012$, respectively), however, 20% cut-off had the higher hazard ratio. Using 10% cut-off of Ki-67, low and high proliferative subgroups had no significant prognostic difference. In hormone receptor positive subgroup, high Ki-67 LI with cut-off 20% were associated with poor breast cancer specific survival ($p=0.015$).

Conclusion : Ki-67 LI with 20% cut-off has the prognostic significance, especially in hormone receptor positive subgroup. Ki-67 LI with 20% cut-off also has the high concordance between manual and eyeballing evaluation.

PO06-09

YOUNGER AGE AND TRIPLE-NEGATIVE BREAST CANCER IN ASSAMESE WOMEN

Gayatri Gogoi[1*], **Mondita Borgohain**[1], **Sa Fazal**[2], **Projnan Saikia**[1], **Ram Kanta Hazarika**[1]

[1] *Dept. of Pathology, Assam Medical College, India*
[2] *Dept. of Surgery, Assam Medical College, India*

Background/Purpose : Breast cancer is the most common female cancer. More than 1 million women worldwide are affected by this diagnosis and 400,000 patients die due to the disease every year. Implementation of mammography screening as well as improvement of adjuvant systemic treatment and a decrease in hormone replacement therapy use have resulted in a decrease in bilateral breast cancer incidence and particularly mortality in developed countries over the past 5 years world-wide, triple-negative breast cancer (TNBC) is characterized by a lack of expression of both estrogen receptor and progesterone receptor as well as HER-2. Thus, to date, chemotherapy remains the only possible therapeutic option. The goal of this study was to evaluate TNBC and correlate clinicopathological parameters with special reference to younger age and identification of prognostic factors that are likely influence prognosis of Assamese women.

Methods : A total of 424 cases of breast cancer diagnosed between July 2010 and June 2013 , 114 patients (27%) were diagnosed with TNBC. The overall survival and disease-free survival were estimated using the Kaplan-Meier method and compared between groups using the log-rank test. Univariate and multivariate analyses were used to identify the prognostic factors, and the prognostic significance of these factors in TNBC patients was reviewed.

Results : The median follow-up time was 27 months. Kaplan-Meier analysis showed significant difference between the tumor subgroups (TNBC vs. non-TNBC) in 3-year overall survival ($p=0.01$) and 5-year disease-free survival ($p<0.01$). Univariate analysis showed that tumor subgroup (TNBC vs. non-TNBC) was a significant predictor of 3-year overall survival and disease-free survival. Age, Tumour type, Tumor size, lymph node status, stage, grade, estrogen receptor status, progesterone receptor status, and HER2/*neu* status and Proliferative index were also significant. In the multivariate analysis, only tumor size, lymph node status, and grade were significantly related to 3-year overall survival and disease-free survival. In TNBC patients, Younger age less than 35 years, Lymph nodal status were significantly related to 3-year overall survival and 3-year disease-free survival.

Conclusion : Average age of breast cancer presentation in Assamese was 44 years in this study . So TNBC cases were significantly higher than other western women and burden of the problem was also due to known chemotherapy resistance. Younger age and positive nodal status were poor prognostic indicator of survival. The molecular profiling of TNBC subgroup can be expected to understand this emerging problem of young women with breast cancer.

PO06-10

THE CLINICAL IMPACT OF PLURIPOTENCY FACTOR LIN28 IN KOREAN BREAST CANCER PATIENT

Sarah Park[1], **Young Kee Shin**[2], **Byung Ju Song**[3], **Byung Ju Chae**[3], **Sang Seol Jung**[3], **Yoon-La Choi**[4*]

[1] *Dept. of Internal Medicine, School of Medicine, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*

[2] *Research Institute of Pharmaceutical Science, College of Pharmacy, Seoul National Univ., Korea*

[3] *Dept. of Surgery, School of Medicine, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea*

[4] *Dept. of Pathology, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : LIN28 is a highly conserved RNA-binding protein emerging as an oncogenic driver in cancer stem cells and modulator of the processing of the let-7 microRNA. The pluripotency factor Lin28 is an RNA-binding protein that is highly expressed in human embryonic stem cells. It can facilitate the reprogramming of human somatic cells to pluripotency with other stem cell marker proteins (Oct4, Nanog and Sox2). Lin28 selectively block the processing of let-7 microRNA (miRNA) (Mirlet7) by recruiting 3' terminal uridylyl transferase (TUTase) in undifferentiated embryonic stem cells. A tumor-suppressor gene, let-7 miRNA, is often down-regulated in various human cancers.

Methods : To define clinical impact of Lin 28 in early breast cancer, we investigated Lin28 expression in tumors from patients with breast cancer who underwent curative resection of tumor. To define prognostic impact of Lin 28 in breast cancer, we investigated Lin28 expression in patients with early breast cancer who underwent curative resection of tumor. In all, 950 slides from paraffin-embedded tissue were available for analysis by Lin28 expression by immunohistochemistry.

Results : 13.2% of cases are identified as Lin28-positive. Lin28 positivity was significantly associated with more advanced stage ($p<0.001$), lymph node involvement ($p<0.001$), absence of estrogen receptor expression ($p=0.002$), negative progesterone receptor expression ($p=0.017$), HER2 overexpression ($p<0.001$), higher histologic grade ($p=0.008$), and higher tumor grade ($p=0.012$). The Lin28 positive patients with early breast cancer demonstrated substantially poorer relapse free survival (Lin28+ vs. Lin28-, $p=0.013$) and trends toward poorer overall survival.

Conclusion : In conclusion, a sub-population of breast cancer with Lin28 expression is significantly associated with aggressive tumor phenotype and poor clinical outcome. LIN28 is selectively expressed in this small fraction of breast cancer cells and targeting LIN28 might be a viable strategy to eradicate cancer stem cell in breast cancer.

PO06-11

PROGNOSTIC SIGNIFICANCE OF THE SERUM HER-2/*NEU* IN PRIMARY INVASIVE BREAST CANCER PATIENTS

Sae Byul Lee, Jongwon Lee, Byungho Son, Seihyun Ahn*

Dept. of Surgery, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea

Background/Purpose : Serum Her-2/*neu* is extracted from the extracellular domain of the Her-2/*neu* tyrosine kinase. It has been shown to have prognostic and predictive information in breast cancer patients. We evaluated the clinical value of the serum Her-2/*neu* concentration and the correlation between the Her-2/*neu* status as determined by immunohistochemical analysis (IHC).

Methods : Serum Her-2/*neu* levels were examined from 3,036 patients with primary breast cancer operation or diagnosis at ASAN Medical Center, Seoul from January 1, 2007 to December 31, 2009. And serum Her-2/*neu* levels were measured by the use of a chemiluminescence immunoassay (ADVIA centaur® system) during the preoperative period. The expression of Her-2/*neu* in all of the breast cancer tissue samples was determined by IHC, and samples with an IHC +2 were subject to fluorescence *in situ* (FISH). When tissue samples exhibited IHC +3 or showed amplification of Her-2/*neu* as determined by FISH analysis, Her-2/*neu* was considered overexpressed. The cut-off value for serum Her-2/*neu* level was 15.2ng/mL.

Results : The mean serum Her-2/*neu* level was 10.2 ng/mL in primary breast cancer samples. The serum Her-2/*neu* concentration significantly correlated with expression of Her-2/*neu* as determined by tissue IHC analysis (grade 1+, 8.96±1.9 ng/mL; grade 2+, 9.71±3.0 ng/mL; grade 3+, 13.42±18.6 ng/mL, $p<0.001$). Increased serum Her-2/*neu* levels were associated with the positivity to lymph node ($p<0.001$), negativity of hormone receptor ($p<0.001$), larger tumor size ($p=0.04$), higher stage ($p<0.001$), higher histologic grade ($p<0.001$), and higher nuclear grade ($p<0.001$) in univariate analysis and they were associated with the negativity of hormone receptor ($p<0.001$), larger tumor size ($p<0.001$), higher stage ($p<0.001$) in multivariate analysis. Serum Her-2/*neu* levels were prognostic factors in disease-free survival (DFS) (normal serum Her-2/*neu*; 59.4 mo, increased serum Her-2/*neu*; 53.5 mo, $p<0.001$) and overall survival (OS) (normal serum Her-2/*neu*; 59.6 mo, increased serum Her-2/*neu*; 52.9 mo, $p<0.001$) in primary breast cancer patients.

Conclusion : Serum Her-2/*neu* appears to be correlated with tissue Her-2/*neu* expression in primary breast cancer. Serum Her-2/*neu* is associated with aggressive clinicopathological features of the primary breast cancer. And increased serum Her-2/*neu* group had a significantly shorter DFS and OS.

PO06-12

EVALUATION OF THE RELATIONSHIP AMONG TOPOISOMERASE II ALPHA EXPRESSION, CHEMOTHERAPEUTIC SENSITIVITY, AND PROGNOSTIC FACTORS IN BREAST CANCER

Hideaki Tokiniwa*, Jun Horiguchi, Daisuke Takata, Mami Kikuchi, Rin Nagaoka, Nana Rokutanda, Ayako Sato, Sayaka Uchida, Misato Ogino, Izumi Takeyoshi

Dept. of Thoracic and Visceral Organ Surgery, Graduate School of Medicine, Gunma Univ., Japan

Background/Purpose：It is important to search for prognostic factors that are useful in estimating an individual patient's risk or to predict response to a specific therapy. Topoisomerase II alpha (Topo IIα) is involved in DNA replication and is a molecular target for anthracycline-based chemotherapy. The collagen gel droplet-embedded culture-drug sensitivity test (CD-DST) is an in vitro chemosensitivity test that has several advantages over conventional tests. The objective of this study was to evaluate of the relationship among Topo IIα expression, chemotherapeutic sensitivity, and prognostic factors in breast cancer.

Methods：CD-DST was performed in 42 patients with breast cancer between July 2001 and December 2002. The specimens obtained during surgery were used for the CD-DST and immunohistological examination of Topo IIα expression. Chemotherapeutic sensitivity to the anticancer drugs epirubicin (EPI), adriamycin (ADM) and 5-FU was estimated using CD-DST. We investigated the correlation of levels of Topo IIα expression within tumor cells were compared with clinicopathological factors and chemotherapeutic sensitivity.

Results：Statistically significant differences were observed between Topo IIα overexpression, nuclear grade (p=0.01), and lymphovascular invasion (p=0.04). Results obtained from the CD-DST showed the chemosensitivity to each anticancer drug to be EPI, 62%; ADM, 40% and 5-FU, 17%. But there was no statistically significant between Topo IIα overexpression and chemosensitivity.

Conclusion：Topo IIα overexpression was associated with poor prognostic factors such as histological grading, a wide lymphovascular invasion. In this study, there was no significance between Topo IIα overexpression and chemosensitivity. And we could not show the role of Topo IIα as a chemosensitivity marker.

PO06-13

PROGNOSIS OF PATIENTS WITH STAGE IV BREAST CANCER WHO UNDERWENT SURGERY

Jun Horiguchi, Daisuke Takata*, Nana Rokutanda*, Rin Nagaoka*, Ayako Sato*, Hideaki Tokiniwa*, Sayaka Uchida*, Misato Ogino*, Mami Kikuchi*, Izumi Takeyoshi*

Dept. of Breast and Endocrine Surgery, Gunma Univ. Hospital, Japan

Background/Purpose : Surgical treatment for primary breast cancer in patients with stage IV breast cancer may improve survival. We determined clinical and pathologic factors affecting overall survival in those who underwent surgery.

Methods : We treated patients with Stage IV breast cancer who underwent surgery in Gunma University Hospital between 1990 and 2005. Total of 56 patients were evaluated, which was 3.8% of all patients who underwent surgery during the same period. We investigated whether factors such as patient age, hormone receptor status, metastatic sites, and number of metastatic sites were associated with overall survival.

Results : Median overall survival was 35 months. Patients under 51 years had a significant better overall survival than those 51 or older (p=0.034). ER (p=0.0014) and PgR (p=0.0004) were favorable prognostic factors for survival. Lung, brain and liver metastases were poor prognostic factors (p=0.0031). Patients with single metastasis had a better overall survival than those with multiple distant metastases (p=0.0086). In multivariate analysis, age, metastatic site and ER were independent prognostic factors for overall survival.

Conclusion : In patients with Stage IV breast cancer who underwent surgery, younger age, hormone receptor-positive breast cancer, and bone or soft tissue metastasis were prognostic factors for overall survival.

PO06-14

DETECTION OF PROGNOSTIC FACTORS IN METASTATIC BREAST CANCER FROM THE RESULT COMPARING CLINICOPATHOLOGICAL FACTORS BETWEEN LONG SURVIVORS AND SHORT SURVIVORS

Keiichi Kontani[1*], **Shin-Ichiro Hashimoto**[1], **Chisa Murazawa**[1], **Shoko Norimura**[2], **Masahiro Ohtani**[3], **Manabu Date**[4], **Hiroyasu Yokomise**[1]

[1] *Dept. of Thoracic, Breast and Endocrine Surgery, Kagawa Univ. Faculty of Medicine, Japan*
[2] *Dept. of Surgery, Japan Red Cross Hospital, Japan*
[3] *Health Care Center, Kagawa Health Service Association, Japan*
[4] *Dept. of Surgery, Date Hospital, Japan*

Background/Purpose : Survival of patients with metastatic breast cancer (MBC) has been significantly prolonged for the last decades due to improvement of anti-cancer therapeutics. However, what patient is expected prolonged survival by treatment remains to be determined.

Methods : To detect prognostic factors in MBC, we compared retrospectively clinicopathologic factors between 23 patients who survived for 50 or more than 50 months after diagnosis with MBC and 28 patients who died in 50 months after diagnosis.

Results : the proportion of hormone receptor (HR)-positive cancer was significantly higher and that of triple negative cancer (TN) was lower in the long survivors than in the short survivors. Metastatic site, number of disease sites, prior chemotherapeutic regimens and HER2 status did not differ between the groups. When a chemotherapeutic regimen which resulted in the most favorable responses among regimens that each patient had received in metastatic settings was compared between the two groups, the proportion of patients who received metronomic regimens was significantly higher in the long survivors than in the short survivors (65.2% vs. 35.7%, $p=0.034$). Overall response rates (ORR) was significantly higher in the long survivor than in the short survivors (82.6% vs. 17.9%, $p<0.00001$). Furthermore, time to treatment failure (TTF), tome to progression (TTP) and overall survival (OS) after receiving the most favorable treatment were significantly longer in the long survivors than in the short survivors. Total number of chemotherapeutic regimens they had received for breast cancer or for MBC did not differ between the groups.

Conclusion : Patients with luminal-type cancer, patients who benefit at least once from chemotherapy including metronomic regimens or patients who receive long-term administration with one regimen can be expected prolonged survival after diagnosis with MBC regardless of number of chemotherapeutic regimens they had received.

PO06-15

CLINICAL SIGNIFICANCE OF OCCULT METASTASES IN SENTINEL LYMPH NODES AMONG BREAST CANCER PATIENTS

Takeshi Nagashima*, Masahiro Sakakibara, Takafumi Sangai, Hiroshi Fujimoto, Hiroshi Suzuki, Masaru Miyazaki

Dept. of General Surgery, Graduate School of Medicine, Chiba Univ., Japan

Background/Purpose：The present study attempts to clarify the clinical significance of occult metastases in sentinel lymph nodes among breast cancer patients.

Methods：The subjects consisted of 1043 cases with clinically node-negative breast cancer who had undergone sentinel node biopsy. Postoperative pathological examination revealed 49 cases with occult metastases (26 isolated tumor cells and 23 micrometastases), despite negative intraoperative results. Distant and local relapses among these patients were reviewed and evaluated.

Results：At a median follow-up of 75 months, eight cases with occult metastases developed recurrences. Axillary and distant relapse rates were 8.2% respectively, which were significantly higher than node-negative cases ($p<0.001$). The relapse rates were not associated with the size of occult metastases. When the occult metastasized cases were treated with no further axillary surgery, the relapse rate was not increased compared with the cases that were diagnosed sentinel node involvements intraoperatively and received sequential axillary dissection.

Conclusion：However occult metastases in sentinel nodes have a little impact for axillary and distant relapse, sentinel lymph node biopsy alone with no further axillary surgery is an appropriate procedure for breast cancer patients with sentinel node occult metastases.

PO06-16

CIRCULATING HER2 EXTRACELLULAR DOMAIN PREDICTS A POOR PROGNOSIS FOR METASTATIC BREAST CANCER PATIENTS

Yasuhiro Suzuki*

Dept. of Breast and Endocrine Surgery, Tokai Univ., Japan

Background/Purpose：Determination of the HER2 status of breast tumor is emphasized in various national guidelines as a necessary step for diagnosis of breast cancer. Detection of serum-soluble-HER2 extracellular domain (HER2-ECD) and establishment of its potential clinical usefulness has created much debate. We assessed whether identification of HER2-ECD have clinical usefulness for metastatic breast cancer.

Methods：Seventy nine breast cancer patients (73 patients were metastatic, 6 patients were locally advanced) who treated in our hospital from May 2010 to March 2012 were identified. HER2-ECD was measured by using new chemilumi-Centaur-HER2/*neu* system (Siemens healthcare diagnostics company Ltd.). HER2-ECD, CEA and CA15-3 were measured from same blood sample. Anti HER2 therapy was allowed in HER2 positive patients.

Results：We analyzed 79 patients in which the median age is 61 years old (range,35-85). 56 patients were HER2 positive (72.7%), 21 patients were negative (27.3%). 42 patients had bone metastasis, 41 patients had lung metastasis and 28 patients had liver metastasis. There were significant differences between HER2-ECD level of distant metastatic patients and no metastasis (bone: $p<0.0257$, lung: $p<0.0219$, liver: $p<0.0194$). In the relationship between treatment response and HER2-ECD, there were significant differences (CR vs. PD, $p<0.0345$). In addition, HER2-ECD level were significant high in expired cases ($p<0.0084$). HER2-ECD was high in combination of CA15-3 comparing with other tumor markers. The Kaplan-Meier graph of overall survival showed significant in the variation of HER2-ECD level. In the group showing of always high HER2-ECD, overall survival was most worth comparing with the group of sometimes high and always normal HER2-ECD ($p<0.001$).

Conclusion：Monitoring of HER2-ECD in metastatic breast cancer patients indicates poor prognosis. HER2-ECD is useful as tumor marker for breast cancer patients.

PO06-17

CANCER STEM CELL MARKER CD49F AND ALDH1 IS ASSOCIATED WITH POOR PROGNOSIS IN HORMONE RECEPTOR (+)/HER2(-) (HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2) BREAST CANCER

Yong Seok Kim, Kyu-Hwa Joo, Jeong-Soo Kim*

Dept. of Surgery, The Catholic Univ. of Korea Uijungbu St. Mary Hospital, Korea

Background/Purpose : Cancer stem cells are characterized by self-renew, tumorigenesis, recurrence and metastasis. Recent studies have shown that the expression of stem cell markers is associated with poor clinical outcome in breast cancer. These markers are correlated with basal-like subtype, mostly but hormone receptor(HR)(+) /HER2(-) breast cancer are not. The purpose of this study was to investigate the correlation between the expression of cancer stem cell marker CD49f and ALDH1 and clinicopathological variables, and clinical outcomes in HR(+)/HER(-) breast cancer patients.

Methods : A total of 164 primary breast cancer patients with hormonal receptor (estrogen or progesterone receptor positive and HER2 negative who underwent breast cancer surgery in our hospital from December 2004 to December 2010 were examined. Expression of CD49f and ALDH1 were accessed by immunohistochemistry on a tissue microarray. We investigated the prognostic factors of stem cell markers using Kaplan-Meier analysis and Cox proportional hazards model.

Results : The median age and follow-up period of the patients was 51.23 years (range 26-84) and 60.42 months (range 5-101), respectively. The expression of CD49f and ALDH1 were 40.9% and 14.6%, respectively. CD49f expression was significantly correlated with histological type-invasive ductal carcinoma ($p=0.027$), lymphatic invasion ($p<0.001$). In Kaplan-Meier analyses, The expression of CD49f was associated with significantly worse disease free survival (DFS) and overall survival (OS)($p=0.023$ and $p=0.009$, respectively). The expression of ALDH1 was associated with significantly worse DFS and OS ($p=0.034$ and $p=0.038$, respectively). A multivariate Cox analysis revealed that the expression of CD49f and lymphatic invasion were independent prognostic factors for DFS and OS.

Conclusion : Unlike current studies, CD49f and ALDH1 status are correlated with poor disease free survival and overall survival in HR(+)/HER2(-) breast cancer patients. This findings suggested CD49f may be a useful marker that used in the prognostic evaluation of patients with HR(+)/HER2(-) breast cancer.

PO06-18

HIGH LEVELS OF APE1 CORRELATES WITH LUMINAL SUBTYPE A BREAST CANCER

Joohyun Woo[1], **Heejung Park**[2], **Anbok Lee**[1], **Sun Young Min**[1], **Cholhee Yun**[1], **Yun-Seok Kim**[1], **Seungwon Yu**[1], **Namsun Paik**[3], **Byung-In Moon**[3], **Woosung Lim**[1*], **Sun Hee Sung**[2]

[1] *Dept. of Surgery, Ewha Womans Univ. Mokdong Hospital, Korea*
[2] *Dept. of Pathology, Ewha Womans Univ. Mokdong Hospital, Korea*
[3] *Division of Breast Surgery, School of Medicine, Ewha Womans Univ., Korea*

Background/Purpose : Human apurinic/apyrimidinic endonuclease 1 (APE1/HAP1/Ref-1) is an essential protein for DNA base excision repair and redox regulation. The ability of cancer cells to recognize DNA damage and initiate DNA repair is an important mechanism for therapeutic resistance. Several recent studies in human tumors suggest that APE1 expression levels and/or subcellular dysregulation may be used to indicate the sensitivity of the tumor toward radiotherapy or chemotherapy. In this study, we assessed the prognostic significance of APE1 and differences of APE1 expression levels according to molecular subtypes in breast cancer of Korean women.

Methods : We analyzed the formalin-fixed, paraffin-embedded tissue sections included tumor from 108 cases diagnosed as invasive breast cancer in Ewha Womans University Medical Center between January 2003 and December 2008. Immunohistochemistry was performed employing the standard streptavidin-biotin complex method. The nuclear level of APE1 was scored by considering the percentage of positive cells. The medical records were reviewed to investigate clinicopathologic characteristics.

Results : We found that nuclear APE1 high expression (proportion≥50%) in breast cancer shows a tendency towards unfavorable prognosis regarding disease free survival (p=0.091). However, there was no significant difference in overall survival between low expression and high expression groups (p=0.309). Significant positive correlation was observed between APE1 nuclear expression and ER status (48.0% vs. 72.3%, p=0.024) and PR status (48.0% vs. 68.7%, p=0.025). Also luminal A was the most commonly observed of molecular subtypes in APE1 high expression group (31.8% vs. 64.1%, p=0.001). P53 and Ki-67 were negatively associated with nuclear APE1 expression (r=-0.218, p=0.029 and r=-0.388, p<0.001, respectively).

Conclusion : This study suggests that APE1 high expression may be represented with poor prognosis in breast cancer. APE1 may be considered as a novel target of treatment in breast cancer to overpower the resistance to current treatment especially in luminal A breast cancer. With larger studies are needed to overcome the limitation of small sample size, it is expected that APE1 would have a more significant value as a prognostic factor in breast cancer.

PO06-19

LONG-TERM SURVIVAL OF DUCTAL CARCINOMA IN SITU OF THE BREAST ACCORDING TO MOLECULAR SUBTYPES

Hee Yong Kwak, Byung Joo Chae, Yong Hwa Eom, Young Ran Hong, Jae Beom Seo, Ja Seong Bae, Byung Joo Song*, Sang Seol Jung

Dept. of Surgery, College of Medicine, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Background/Purpose : Ductal carcinoma *in situ* (DCIS) is a non-invasive breast cancer with little risk of local recurrence. Increasing evidence suggests that biomarker expression in cancer patients influences response to treatment and prognosis after treatment. The aim of this study was to evaluate whether molecular subtypes of the breast cancer affected long-term survival.

Methods : A database of 370 patients who underwent breast surgery with the diagnosis of DCIS or suspicious for DCIS, by either excision biopsy or core needle biopsy, enrolled between January 1991 and December 2010 was reviewed. Those with secondary cancer, follow-up loss, invasive breast cancer or benign breast mass on final pathology were excluded. Probability of local recurrence was calculated using the Kaplan-Meier method and compared with log rank test.

Results : A total of 265 patients with pure DCIS were treated with mastectomy (n=101, 38.0%) or breast-conserving surgery (BCS) plus radiation (n=164, 62.0%). Median follow-up was 72 months (range, 11-266 months). Patients with hormone receptor, either estrogen receptor (ER) or progesterone receptor (PR), positive were given tamoxifen 20 mg daily for 5 years. Local recurrence was significantly associated with larger size (p=0.034, 95% CI 1.021-1.708), comedonecrosis (p=0.017, 95% CI 0.298-0.887), and nuclear grade (p<0.001, 95% CI 1.245-1.920) on multivariate analysis. 10-year disease-free survival was 89.5%, 80.4%, 90.3% for Luminal, HER2, triple-negative subtypes, respectively (p=0.585). There also was no statistically significant difference between molecular subtypes in terms of ipsilateral breast tumor recurrence (p=0.756) and contralateral breast tumor recurrence (p=0.450).

Conclusion : Local recurrence after DCIS treatment could be a dreadful event which could affect long-term prognosis. HER2 DCIS showed almost doubled, however not statistically significant risk for local recurrence. Therefore, HER2 DCIS especially, should be monitored with more close surveillance for local recurrence after the treatment.

PO06-20

CAN LOCAL TREATMENT FOR BRAIN METASTASIS BRING A SURVIVAL BENEFIT IN BREAST CANCER PATIENTS?

Jae Uk Chong, Sung Gwe Ahn, Hak Min Lee, Seung Ah Lee, Joon Jeong*

Dept. of Surgery, College of Medicine, Yonsei Univ., Korea

Background/Purpose : To investigate survival patterns after brain metastasis and recognize prognostic factors for breast cancer patients with brain metastasis, we performed this analysis.

Methods : A retrospective review of breast cancer patients diagnosed with brain metastasis between January 2005 and December 2012 at a single institute was conducted. Treatment details and tumor characteristics were investigated. Types of local treatment for brain metastasis included surgery, radiotherapy, combined therapy and no treatment. We evaluated overall survival after brain metastasis (OSBM), brain metastasis-specific survival (BMSS) and brain metastasis-specific progression free survival (BMPFS). Survival analysis was performed using log-rank test and a Cox proportional hazard regression model.

Results : A total of 56 patients were identified. Results of treatment on survival showed no significant benefit in OSBM (p=0.105), while BMSS and BMPFS showed survival benefit (p=0.027 and p=0.033, respectively) in treatment group. On univariate analysis, presence of estrogen receptor in primary breast cancer showed a survival benefit in OSBM (p=0.021) and BMSS (p=0.027). Results also showed that low histologic grade was associated with survival benefit in BMSS (p=0.006) and BMPFS (p=0.002). On multivariate analysis for OSBM, local treatment of brain metastasis had no prognostic value, but positive estrogen receptor status was demonstrated as a significant prognostic factor. On multivariate analysis for BMSS and BMPFS, low histologic grade and local treatment of brain metastasis were revealed as significant prognostic factors.

Conclusion : Our findings suggest that local treatment of brain metastasis could potentially bring a survival benefit in patients without life threatening distant metastasis. Especially, in patients with positive estrogen receptor and low histologic grade of primary breast cancer, active local treatment of brain metastasis could result in favorable outcome.

PO06-21

SERUM EPIDERMAL GROWTH FACTOR IS ASSOCIATED WITH PROGNOSIS AND HORMONE RECEPTOR STATUS IN PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANCER TREATED WITH FIRST-LINE TRASTUZUMAB PLUS TAXANE CHEMOTHERAPY

Ji-Won Kim[1], **Jee Hyun Kim**[1], **Seock-Ah Im**[1], **Kyung-Hun Lee**[1], **Tae-Yong Kim**[1], **Sae-Won Han**[1], **Yoon Kyung Jeon**[2], **Do-Youn Oh**[1], **Tae-You Kim**[1], **In Ae Park**[2]

[1] *Dept. of Internal Medicine, College of Medicine, Seoul National Univ., Korea*
[2] *Dept. of Pathology, College of Medicine, Seoul National Univ., Korea*

Background/Purpose : Epidermal growth factor (EGF) is a ligand for the epidermal growth factor receptor (EGFR). Human epidermal growth factor receptor 2 (HER2) shares common signal pathways and forms a heterodimer with EGFR. In this study, we investigated the clinical and pathologic implications of serum EGF levels in patients with HER2-positive metastatic breast cancer (MBC).

Methods : We analyzed serum EGF levels from baseline serum samples of consecutive patients with HER2-positive MBC who received first-line trastuzumab plus taxane chemotherapy, and correlated them with treatment outcomes and pathologic features.

Results : A total of 50 women were analyzed. The median age was 47 years (range, 27-72 years). Patients with high serum EGF levels (≥10.0 pg/mL) had significantly longer overall survival (47.0 months (95% CI=28.3-65.7 months) vs. 23.3 months (95% CI=13.5-33.1 months, p=0.009) with a tendency toward longer progression-free survival (p=0.123). The multivariate analysis revealed that high serum EGF level (≥10.0 pg/mL) was a significant factor for longer OS (hazard ratio 0.24 [95% CI= 0.07-0.76], p=0.016). Serum EGF levels were not associated with hematologic or cardiac adverse events. Estrogen receptor (ER)-positive patients tended to have higher serum EGF levels than ER-negative patients (18.8 pg/mL [range, 0.0-69.0 pg/mL] vs. 13.7 pg/mL [range, 0.0-59.5 pg/mL], p=0.309). In addition, progesterone receptor (PgR)-positive patients had significantly higher serum EGF levels than PgR-negative patients (24.3 pg/mL [range, 9.5-69.0 pg/mL] vs. 12.3 pg/mL [range, 0.0-59.5 pg/mL], p=0.006).

Conclusion : Our data suggest that high serum EGF levels may be associated with good prognosis in patients with HER2-positive MBC receiving trastuzumab plus taxane chemotherapy. In addition, serum EGF levels were associated with PgR positivity.

PO06-22

WHICH ONE IS MORE IMPORTANT PROGNOSTIC FACTOR OF BREAST CANCER? : GOOD BIOLOGIC SUBTYPE OR EARLY STAGE

Hyosun Kim, Kiseok Shin, Hyeah Shin Shin, Sun-Hee Kang*

Dept. of Breast Endocrine Surgery, School of Medicine, Keimyung Univ. Dongsan Medical Center, Korea

Background/Purpose : Nodal involvement with cancer cell has been one of the most important prognostic factors. Recent decades, risk stratification has been largely changed according to hormone receptor status and HER2 status which is now affecting the adjuvant treatment. In this study, we compared the prognostic power of intrinsic subtype with nodal involvement.

Methods : We reviewed the medical records of the patients who had a curative surgery for breast malignancy between 2003 and 2009 in our institute. Five hundred eleven patients who were pathologically node negative or N1 stage were included. We analyzed clinicopathologic factors such as age, tumor size, stage, histologic grade, nuclear grade, hormonal receptor status, HER2, adjuvant treatment, recurrence and survival. Disease free survival (DFS) and overall survival (OS) were analyzed using Kaplan-Meier curve, log rank test and Cox regression model.

Results : Node negative group was composed of 363 patients and pN1 group was composed of 148 patients of total 511 patients. Five year DFS was 90.7% and 5 year OS was 97% over median 58 months of follow-up. N1 group showed statistically worse 5 year DFS than N0 group (87.2% vs. 92.1%, HR 2.26, p=0.005). Triple negative subgroup showed statistically worse 5 year DFS than luminal A subtype (81.9% vs. 93.8%, HR 2.78, p=0.001). N1 stage with luminal A group showed better DFS than node negative triple negative subtype compared with node negative luminal A subtype (5 year DFS 93.2%, HR 1.581 vs. 5 year DFS 86.4%, HR 2.185) but not statistically significant (p=0.293 and p=0.066, respectively). N1 stage with triple negative subtype showed worst DFS (5 year DFS 67.8%, HR 6.073).

Conclusion : Node negative and triple negative breast cancer showed inferior DFS than pN1 stage with luminal A subtype. However fewer patients (77.1%) of node negative and triple negative subtype had chemotherapy compared with patients who had chemotherapy in N1 stage with luminal A subtype (89.1%). We have to decide adjuvant chemotherapeutic agent according to not only the nodal status but also the intrinsic subtype.

PO06-23

A LONGITUDINAL STUDY OF SELF-EFFICACY, DEPRESSION, AND POSTTRAUMATIC GROWTH IN BREAST CANCER SURVIVORS PARTICIPATING BREAST HEALTH EDUCATIONAL ACTIVITIES (HAN-U-YE-KANG PROGRAM)

Myungsun Yi, Jieun Cha*, Young Mi Ryu

College of Nursing, Seoul National Univ., Korea

Background/Purpose : Han-U-Ye-Kang Program has been conducted annually at the Seoul National University College of Nursing from 2004. Each year, about 20 breast cancer survivors were trained as voluntary breast health educators. They were trained in principles of health education, creating general knowledge of breast cancer and breast self-examination. According to the 'helper-therapy principle' by Riessman, giving help to others predicted improvements in psychosocial adjustment. Helping others has a therapeutic effect. This present work explores the impact of helping others through Han-U-Ye-Kang educational activities on the psychosocial outcomes of the provider.

Methods : This exploratory study utilized a longitudinal design. Subjects were 14 breast cancer survivors who participated in the Breast Health Educational Program. The data were collected between February and May in 2013. Self-report questionnaires were used to measure the self-efficacy for breast cancer, depression, and posttraumatic growth (PTG) at pre-education (T0), and at 1 month (T1) and 3 months (T2) post-education. A generalized estimating equation (GEE) regression model was used to identify the effects.

Results : The average age of the subjects was 50.0 and an average of 63.5 months following diagnosis. The mean number of educational activities were 1.08 (T1), 2.71 (T2). The score of self-efficacy were 48.86 (T0), 51.62 (T1), 50.07 (T2), depression were 9.21 (T0), 8.31 (T1), 5.64 (T2), and PTG were 63.21 (T0), 61.92 (T1), 62.50 (T2). However, GEE analysis showed that the increase in self-care efficacy ($p=0.056$) and PTG ($p=0.540$), and decrease in depression ($p=0.224$) within 1 month and 3 months after education program were not statistically significant.

Conclusion : The results indicated that psychosocial outcomes of breast cancer survivors remained stable over time regardless of educational volunteering activities. Limitation of this study might result from a small sample size and participants who had fairly high levels of psychosocial well-being compared with general population and other breast cancer survivors. However, three month of follow-up after completion of a breast health education program may be too short to gain insights into impact on well-being. Further studies are needed to examine its effects over a longer period of time for more vulnerable groups.

PO07-01

THYROID METASTASIS FROM BREAST CARCINOMA ACCOMPANIED WITH PAPILLARY THYROID CARCINOMA

Kwang Kuk Park, Song-I Yang, Dong-Won Ryu, Jeong-Hoon Kim*

Dept. of Surgery, College of Medicine, Kosin Univ., Korea

Background/Purpose : Metastases to the thyroid gland are very rare. The most common primary sites of metastatic thyroid tumors are malignant melanoma, kidney, breast and lung cancer. Additionally, to the best of our knowledge, there is no reported case of a thyroid metastasis from breast carcinoma accompanied with papillary thyroid carcinoma.

Methods : A 51-year-old female patient was presented with palpated lymph node on left lateral neck. The patient underwent a left modified radical mastectomy followed chemotherapy and hormonal therapy in 8 years ago. In fine needle aspiration, left thyroid was diagnosed with papillary thyroid carcinoma. The patient had total thyroidectomy with lateral neck node dissection. Pathologic assessment of the specimen showed metastatic carcinoma from the breast carcinoma and papillary thyroid carcinoma. Histologically, large tumor cells in the right and left lobes are exhibited negative staining for the estrogen receptor, progesterone receptor and positive for C-erb-B2 (2+), similar to the staining pattern of the primary breast lesion. And cytokeratin 19, HBME-1 and TTF-1 are negative. The patient was scheduled to receive systemic chemotherapy with TA (75 mg/m^2 taxotere and 50 mg/m^2 doxorubicin every 2 weeks).

Results : The patient had stable disease after operation and chemotherapy.

Conclusion : Although thyroid gland are uncommon metastatic site. A diagnosis of metastatic disease should be considered in a patient with previous history of malignancy.

PO07-02

BREAST METASTASIS OF NON-SMALL CELL LUNG CANCER

Kyung-Hee Lee, Tae-Ryung Kim, Kwan-Il Kim, Heung-Kyu Park*

Dept. of Surgery, Breast Cancer Center, Gachon Univ. Gill Hospital, Korea

Background/Purpose : Breast is an uncommon site for metastatic disease. The most common disease metastasizing to breast is contralateral breast cancer. Considering the breast metastasis originated from other organ except contralateral breast, malignant melanoma and lymphoma are most common cause. Especially, breast metastasis caused by non-small cell lung cancer (NSCLC) is relatively rare.

Methods : We recently experienced a case of a 55-year-old female patient with breast metastasis of NSCLC.

Results : She was diagnosed as NSCLC of left lung in 2001, and had left upper lobectomy. She was treated with etoposide and cisplatin combination chemotherapy and radiotherapy. After 55 months, her NSCLC was recurred. Since then, she should undergo five types of chemotherapy and two operations because of recurrence and the side effect of chemotherapy. At March 2013, she complained the palpable breast mass with fourth recurrence, and was referred to our breast clinic. She had a 1 cm sized, round, hypoechoic mass in lower inner portion of left breast. Ultrasound-guided biopsy revealed it is the metastasis of pulmonary origin. She was treated by the wedge resection of left lower lobe of lung and the wide excision for breast mass.

Conclusion : We report the case of metastatic breast cancer from NSCLC with a review of the literature.

PO07-03

CASE SERIES OF MALE BREAST CANCER IN SINGAPORE IN A TERTIARY INSTITUTION: OUR EXPERIENCE

Chi Wei Mok, Siew Kuan Lim, Wai Peng Lee, Su-Ming Tan

Dept. of General Surgery, Changi General Hospital, Singapore

Background/Purpose：Male breast cancer remains a rare but nonetheless important disease entity. Owing to its rarity, there is little data in the literature especially in the Asian context. This study aims to review cases of male breast cancer in our institution over the past 15 years.

Methods：All consecutive male subjects with histologically proven breast cancer from a prospectively collected database over a 15 years duration (1998 to 2013) were identified and included in the study. Data on demographics, clinical presentation, tumour characteristics, and treatment as well as survival data were then retrospectively reviewed.

Results：A total of 7 cases (0.3%) of male breast cancer were identified from a pool of 2081 subjects with breast cancer diagnosed in our institution from 1998 to 2013. The median age of patients was 64 (41-78) years old and all subjects except one were Chinese. All subjects presented with a breast lump. Clinical assessment revealed a suspicious lump in only one patient; another patient had a lump that was thought to be benign whereas the remaining five patients had lumps that were indeterminate in nature. All patients proceeded with a fine needle aspiration of their lumps and results showed inconclusive findings for one patient, atypical/suspicious cells in three patients, malignant in the remaining three patients. The patient with inconclusive findings proceeded with a core biopsy which was reported as malignant. With regards to tumour characteristics, four patients showed pure infiltrating ductal carcinoma on histology, another patient had features of infiltrating ductal carcinoma with mucinous component whereas the last patient had invasive papillary carcinoma on histology. Only three patients had nodal involvement at presentation with four patients having an overall stage of 2 and above. All patients showed an overexpression of ER and PR receptors while only one showed Her-2 receptor overexpression. Five patients underwent simple mastectomy and axillary clearance of which one of these five patients had an initial sentinel lymph node biopsy performed which was found to be positive and subsequently went on to have an axillary clearance. All patients except one who received mastectomy went on to have adjuvant (chemotherapy or hormonal) therapy. The only patient who did not receive adjuvant therapy had Stage I disease and he was offered adjuvant hormonal therapy but declined. The rest of the patients had Stage II disease. At the time of writing, five patients are alive while two patients succumbed to their disease. Median survival of patients in our series is 6.8 years.

Conclusion：From our series of male breast cancer patients over a period of 15 years, all patients presented with breast lumps. None had nipple discharge or pain as the first presenting complaint. Infiltrating ductal carcinoma is the most common histological subtype and all patients have tumours with an overexpression of estrogen and progesterone receptors. Simple mastectomy and axillary sampling or clearance remains the standard of care for patients in our series in terms of surgical management. Adjuvant therapy is offered to 5 patients. The only patient with Stage I disease was offered adjuvant hormonal therapy but declined.

PO07-04

PRIMARY SMALL CELL CARCINOMA OF THE BREAST

Kwang Kuk Park, Song-I Yang, Chung-Han Lee, Dong-Won Ryu*

Dept. of Surgery, College of Medicine, Kosin Univ., Korea

Background/Purpose : Primary SCC of the breast accounts for less than 1% of primary breast cancers. Due to the rarity of this type of tumor and the lack of a standard treatment, we report here a case study of primary SCC of the breast and discuss its clinicopathologic characteristics.

Methods : A 58-year-old female patient presented with a painless mass in right breast for 2 months. An ultrasound scan revealed two solid and low heterogeneous echoes in the left breast: one was in the 3 o'clock position, 35 mm away from the nipple. A mass was poorly defined with irregular borders. She underwent modified radical mastectomy with axillary lymph node dissection. Microscopically, the mass (in the 3 o'clock position, 35 mm away from the nipple) was about 2.2 cm × 1.8 cm × 1.6 cm, which was diagnosed histologically small cell carcinoma with glandular differentiation. Immunohistochemically, tumor cells were negative for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 and histological examination also demonstrated 1 positive lymph node out of 25 axillary lymph nodes. The patient was scheduled to receive systemic chemotherapy with doxorubicin-cyclophosphamide followed by docetaxel every 3 weeks (60 mg/m^2 doxorubicin, 600 mg/m^2 cyclophosphamide and 75 mg/m^2 docetaxel).

Results : The patient is currently free of disease 42 months after operation with adjuvant chemotherapy.

Conclusion : In this report, we describe a case of primary small cell carcinoma of the breast.

PO07-05

DUCTAL CARCINOMA *IN SITU* ARISING IN JUVENILE FIBROADENOMA: A CASE REPORT

Sinill Kim, Seung Pil Jung, Hye Yoon Lee, Hoon Yub Kim, Jeoung Won Bae*

Division of Breast and Endocrine Surgery, College of Medicine, Korea Univ. Hospital, Korea

Background/Purpose : Fibroadenoma is the most common breast tumor in women younger than 30 years. Fibroadenoma is generally considered benign. Carcinoma arising within a fibroadenoma is rare. Especially, malignant transformation of juvenile fibroadenoma is of great rarity. So we report this case.

Methods : A 36-year old woman with no family history of breast cancer was admitted for an oval, hard and palpable mass with tenderness in right breast at 3 o'clock. Gun biopsy was performed for histologic diagnosis preoperatively. The tumor was diagnosed as ductal carcinoma in situ arising in juvenile fibroadenoma.

Results : Breast wide excision with sentinel lymph node biopsy was performed. The negative margin of the resected specimen and no metastasis were in the sentinel nodes. Histopathological analysis revealed ductal carcinoma *in situ* growed into ducts and lobules, replacing the ductal luminal cells of fibroadenoma, which showed glandular and cellular stromal elements. Immunohistochemistry revealed the tumor to be estrogen receptor positive (>95%), progesterone receptor positive (>95%), p63 positive and negative for c-erb-B2, CK5/6, EGFR and Ki-67 (labeling index <1%). Our further treatment plan is tamoxifen for 5 years and radiation therapy.

Conclusion : To add further evaluation on this disease, we report our experience about this rare disease.

PO07-06

CASE REPORT: METACHRONOUS BREAST CANCER WITH DIFFERENT HISTOPATHOLOGICAL FINDINGS

Seung Jo Choi, Jeonghui Lee, Min Sung Chung*

Dept. of Surgery, Hanyang Univ. Medical Center, Korea

Background/Purpose : Metaplastic carcinoma of breast is rare which occurs in less than 1?5% of breast carcinoma patients. Within their lifetime, 2-20% of breast cancer patients develop a new tumor in their contralateral breast. In this report, we present the rare case of metachronous breast cancer in young female who has different histopathological findings.

Methods : 29 year old young women was diagnosed as right breast cancer on October 1st 2008 and underwent breast conserving surgery with axillary lymph node dissection. Histopathology was metaplastic breast cancer with feature of adenosquamous carcinoma. No lymph node was involved. Estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 statuses were tested by immunohistochemistry (IHC), and were all negative.

Results : During scheduled 6 month follow-up with mammography and breast sonography, there was no evidence of locoregional recurrence and contralateral breast was within normal finding as well. During our short term follow-up, palpable mass was developed in the contralateral breast in May of 2013. 4.7cm irregular hypoechoic mass was detected by ultrasonography and invasive ductal carcinoma was diagnosed with core needle biopsy. Several lymph nodes enlargement in the left axilla level I were found on the breast MRI and PET-CT. Patient then underwent bilateral skin sparing mastectomy with left axillary lymph node dissection and immediate reconstruction with TRAM flap was performed. 4.5cm invasive ductal carcinoma with lymph node metastases in the left axilla was removed with negative margin and by IHC, all receptors were negative.

Conclusion : A case of metaplastic carcinoma of breast with *BRCA-1* mutation was first reported in 2007. Moreover there was a report of metaplastic breast carcinomas which have basal-like immunophenotype. In this case, *BRCA* mutation was not tested at the time of first surgery, however *BRCA*1 mutation was detected on the second surgery, while both tumors were 'triple negative'. This case could be the informative experience to study the relationship among metaplastic carcinoma, triple negative breast cancer and *BRCA* gene mutation.

PO07-07

DISTANT METASTASIS WITHOUT INTERVENING INTRABREAST TUMOR RECURRENCE AFTER BREAST CONSERVING SURGERY FOR DUCTAL CARCINOMA *IN SITU*

Hye A Shin[1], **Sun Young Kwon**[2], **Ki Suck Shin**[1], **Hyo Sun Kim**[1], **Sun Hee Kang**[1*]

[1] *Dept. of Surgery, Keimyung Univ., Korea*
[2] *Dept. of Pathology, Keimyung Univ., Korea*

Background/Purpose : The recurrence pattern of ductal carcinoma *in situ* (DCIS) is usually in breast and it can be DCIS or invasive ductal carcinoma. Isolated distant metastasis without ipsilateral breast tumor recurrence is very rare. Here, we report a case of isolated distant metastasis of DCIS.

Methods : Forty seven year-old female patient came to our hospital due to a palpable mass on her left breast. Breast image and core needle biopsy showed ductal carcinoma in situ, solid type.

Results : We performed a breast-conserving procedure with sentinel node biopsy at December 2009. Final pathologic result showed 1.8cm sized, pure DCIS, solid type, high nuclear grade, punctuate necrosis present. Immunohistochemistry (IHC) of DCIS showed as estrogen receptor is strong positive, progesterone receptor negative, HER2 status is strong positive. Two sentinel nodes were harvested and none of them showed malignant cell. Whole breast radiotherapy was done with dose of 5040cGy at left breast and 1600cGy at tumor bed. Tamoxifen was prescribed but she did not take it regularly. After completion of radiotherapy, she checked her breast by MMG and USG. Last follow-up breast image was performed at 12 March 2012 and showed no evidence of recurrence. At April 2013, she visited for regular breast check. She took breast USG and MMG. However the breast USG showed round isoechoic, 23mm sized abnormally enlarged lymph node in left supraclavicular area. We did fine needle aspiration biopsy on the supraclavicular lymph node, the cytologic result showed atypical cell. Breast MRI, MMG and USG did not show any evidence of ipsilateral breast recurrence. We ordered neck CT and chest CT to assess lung malignancy, the results of CT showed there was no sign of lung malignancy, but incidentally found multiple hepatic mass. And then she took a liver CT with hepatic biopsy. The pathlogic result of liver showed metastatic carcinoma and immunohistochemistry of estrogen receptor showed strong positive. She started systemic chemotherapy with taxane based regimen. Retrospectively, two pathologists reviewed the slides of previous operation tissues, they could not find any focus of invasive component.

Conclusion : We reported a case of hepatic metastasis without intervening breast recurrence from pure DCIS, her disease free interval is about 4 years.

PO07-08

METASTATIC MALIGNANT PERIPHERAL NERVE SHEATH TUMOR IN BREAST: A CASE REPORT

Chang Hyun Shin, Jae Il Kim*

Dept. of Surgery, College of Medicine, Inje Univ., Ilsan Paik Hospital, Korea

Background/Purpose : Malignant peripheral nerve sheath tumor is a rare soft tissue sarcoma of ectomesenchymal origin. It is the malignant counterpart of benign soft tissue tumors like neurofibromas and Schwannomas and may often follow them. Breast is an extremely rare location of this lesion.

Methods : A-28-year-old woman who had been diagnosed with type II neurofibromatosis and mediastinal malignant peripheral nerve sheath tumor presented with enlarging painless lumps in her both breast. On physical examination, about 2.5 x 2.0 cm sized single nodule was palpated on upper outer quadrant of right breast and variable sized multiple nodules were also palpated on her both breast.

Results : Breast ultrasonograhy and chest CT findings were highly suggestive of breast carcinoma or metastasis of known malignant peripheral nerve sheath tumor. She underwent excisional biopsy to confirm the diagnosis.

Conclusion : Pathologic finding revealed metastatic malignant peripheral nerve sheath tumor of right breast and two intraductal papillomas of both breast. She received radiotherapy on right chest wall.

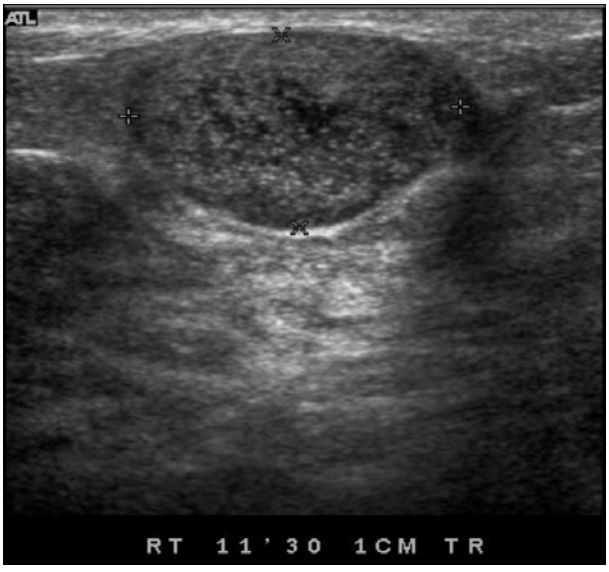

Figure 1

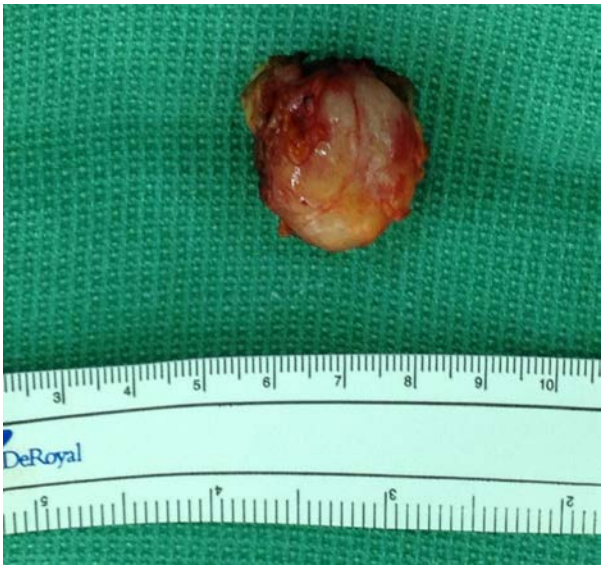

Figure 2

PO07-09

A CASE OF PRIMARY BREAST MALIGNANT MELANOMA AS PRESENTING WITH AN ISOLATED BREAST TUMOR

Eunhye Choi

Dept. of General Surgery, Presbyterian Medical Center, Korea

Background/Purpose : Primary malignant breast melanoma is extremely rare, especially manifested with a breast mass, not cutaneous lesion. Malignant melanoma in the breast can manifest very different: primary melanoma of the breast skin, melanoma metastasis to the breast, in-transit metastases to breast tissue and breast skin, primary breast melanoma and metastasis in the intramammary lymph nodes. Some said that primary malignant melanomas of the breast and cutaneous melanomas arising in the skin of the breast have been reported. but others said about the possibility that primary melanomas of the skin disappear spontaneously, their metastases being the only clinical finding. Many authors had proposed that a primary melanoma must be a large papillary or polypoid tumor arising from a single pedical at the mucosal surface. Little is known about their biological behavior, and the prognosis is generally less avorable than that of primary cutaneous malignant melanomas because non-cutaneous melanomas are often not discovered until they are at an advanced stage. Where is this patient going?

Methods : A 53-year-old woman came to out institution with a sudden, enlarging mass of right breast in May, 2013. She was being observed with right breast discomfort from November 2011 in out breast clinic. At that time sonography of the breast showed that there is 9x8x4 mm, well-defined, ovoid, anechoic nodule with posterior enhancement at 8 o'clock of right breast in 2011 and 2012. And now there was increasing to 3x2.8x1.5 cm and the mass had lobular contour and angular margin and vascularized soft tissue component internally. The patient underwent sonographic-guided core biopsies. The mass was consistent with malignant melanoma. She was examined whether the melanoma was primary or metastatic. On physical examination, that was soft and unattached to the skin and chest wall, movable and it was not painful in right lower outer quadrant breast. She has been 20x20 cm of congenital nevus at the right chest wall including right breast skin from birth. But in the multiple exisional biopsies, that was only a nevus. Careful examination of the skin and mucous membrane (thorough physical examination , laryngoscopy, EGD, Colonoscopy) did not reveal the focus of a primary malingnant melanoma. In the PET-CT, there were no abnormality and metastasis except the right breast.

Results : She received breast conserving operation and axillary lymphnode dissection. In pathologic report, the breast malignant melanoma had the size of tumor: 2.9x2.5x1.5 cm, no lympho vascular invasion, no involvement of skin and free surgical margins from tumor, and no axillary lymphnode involvement. In the immunestain, there were HMB45(+), S-100(+), CK(-), Vimentin(+), Ki-67 (around 15%). Subsequently, the patient underwent postoperative radiotherapy to the whole breast.

Conclusion : Where is this patient going?

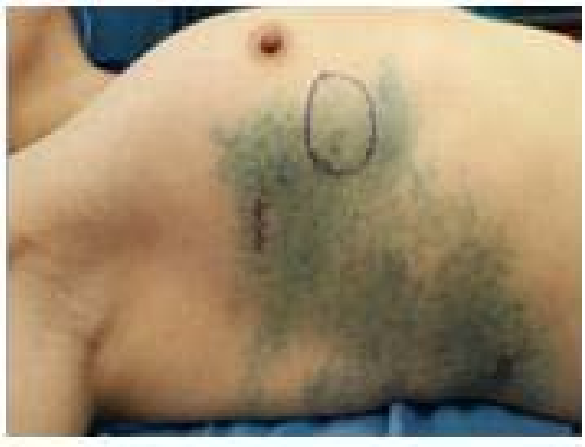

Figure 1

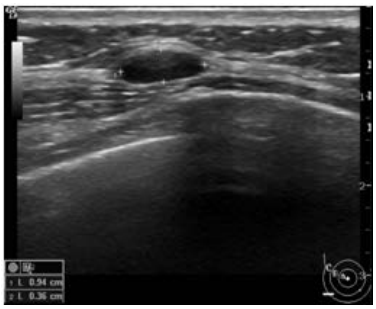

Figure 2

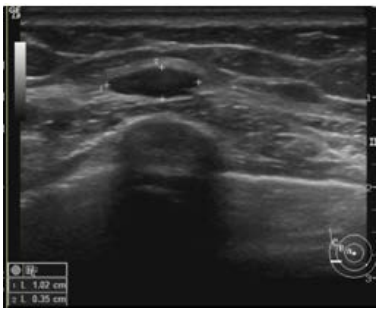

Figure 3

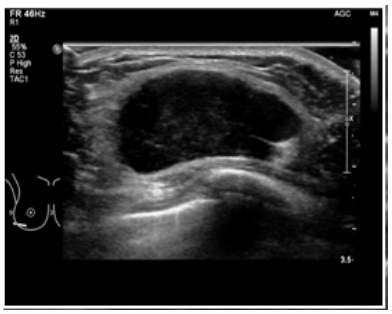

Figure 4

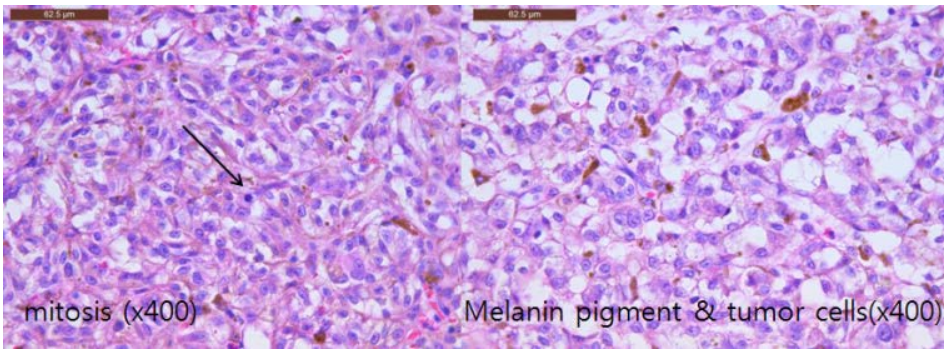

Figure 5

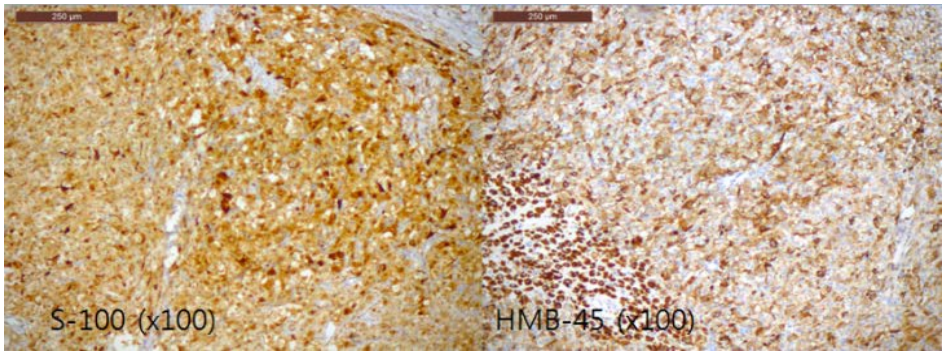

Figure 6

PO08-01

AN ANALYSIS OF THE HOMEPAGES OF ONLINE SHOPPING MALLS FOR BREAST PROSTHESES IN KOREA

Hee Sun Kang

Dept. of Nursing, Chung-Ang Univ., Korea

Background/Purpose : A mastectomy can significantly alter a women's body. Breast prosthesis can help restore balance, posture, and a confident self-image after a mastectomy. The internet has become a popular resource for health information and medical products for cancer survivors. The purpose of this study was to examine the composition and contents of the homepage of online shopping malls for breast prostheses in Korea.

Methods : This study was a cross-sectional descriptive study focusing exclusively on Web sites that included the phrase "breast prosthesis" in their product descriptions. Seven sites met this inclusion criterion. Data were collected through the Web sites and analyzed for content.

Results : There were two types of sites; those, for breast prosthesis products or cancer-related products. The sites were composed of several categories, such as products, information corner, and frequently asked questions. Silicone breast prostheses and mastectomy brassieres were the most commonly sold products online. Information provided on the sites included resources for survivors providing information on exercise after mastectomy, lymphedema prevention, proper fit of prostheses, etc. The most common type of inquiries was related to products. Information on customized products was lacking, and all sites used only one language (Korean). Less than half of the reviewed sites indicated a date of last revision.

Conclusion : Web sites could become useful sources to people seeking electronic information about breast prostheses. Thus, site operators should make efforts to provide more comprehensive information, not only for cancer survivors, but also for their families and caregivers. Information in different languages should also be provided, as needed. Furthermore, clinicians need to be aware that only limited information is being provided on these sites and should therefore be sensitive to the unmet needs of breast cancer survivors and their families.

PO08-03

PSYCHOSOCIAL INTERVENTIONS FOR PSYCHOLOGICAL DISTRESS, SELF CARE AND QUALITY OF LIFE IN CANCER PATIENTS: A META-ANALYSIS

Pok-Ja Oh[1], **Eun Ai Lee**[2]

[1] *Dept. of Nursing, Sahmyook Univ., Korea*
[2] *Dept. of Nursing, Graduate School, Sahmyook Univ., Seoul, Korea*

Background/Purpose : The purpose of this study was to investigate the effects of cognitive behavioral therapy (CBT) on depression, anxiety, self-care behavior and quality of life in cancer patients.

Methods : Published articles and unpublished dissertations between 1980 and 2012 were identified through the 6 electronic databases in Korea. 19 studies met the inclusion criteria with a total of 759 participants. Two authors independently assessed the methodological quality by Cochrane's Risk of Bias and Methodological Items for Non Randomized Studies. The data were analyzed by the RevMan 5.1 program of Cochrane library.

Results : Overall, study quality was moderate to high. CBT was conducted by mean 4.8 weeks, 7.7 sessions and 55-minute per session. CBT was effective for depression (d=-0.85; 95% CI=-1.09 to -0.61), anxiety (d=-0.55; 95% CI=-0.77 to -0.33), self-care behavior (d=-0.97 95% CI=-1.78 to -0.17), and quality of life (d=-0.76; 95% CI=-1.02 to -0.51). Publication bias was not detected as evaluated by funnel plot.

Conclusion : This study suggests that various CBT interventions can assist cancer patients in reducing emotional distress and improving self-care and quality of life.

PO08-04

MINDFULNESS-BASED STRESS REDUCTION PROGRAM (MBSR) FOR ADVANCED BREAST CANCER PATIENTS

Chung Eun Lee[1], **Soohyeon Lee**[2*], **Sang Hee Kim**[3], **Sue Kim**[3], **Hye Myung Joo**[4]

[1] *Medical Oncology Outpatient Unit, College of Nursing, Yonsei Univ. Health System Severance Hospital, Korea*
[2] *Division of Medical Oncology, Dept. of Internal Medicine, College of Medicine, Yonsei Univ., Korea*
[3] *Dept. of Clinical Nursing, College of Nursing, Yonsei Univ., Korea*
[4] *Mindfulness Institute, Korea*

Background/Purpose : The purpose of this study was to describe the effectiveness of the Mindfulness Based Stress Reduction (MBSR) program for improving the physiological and psychological state of advanced cancer patients in an outpatient clinic setting in Korea.

Methods : The pretest-posttest experimental design was applied. The MBSR program was performed from May 14 to July 3 in 2013. The weekly, two hour MBSR program was applied for eight weeks. Twenty-two metastatic breast cancer patients were initially enrolled, but twelve patients dropped out because of poorer general conditions. As such, the final count was ten patients completed for the eight week course. Outcomes included pain (Brief Pain Inventory), anxiety and depression (Hospital Anxiety and Depression Scale, HADS), and distress (Distress Thermometer, DT). The Functional Assessment of Cancer Therapy-Breast (FACT-B) and the Functional Assessment of Cancer Therapy-Endocrine Symptoms (FACT-ES) were measured. Moreover, Heart Rate Variability (HRV), body index, and laboratory data were observed. Data were analyzed with the Wilcoxon signed-rank test.

Results : The median of the Distress thermometer score significantly improved from 5 to 3 (p=0.046) after the MBSR program. The median values of the homeostasis model assessment of insulin resistance (HOMA-IR), fasting insulin, and triglycerides were significantly reduced 27.5 to 12.3 (p=0.028), 5.2 to 3.0 (p=0.018) and 146 to 94, (p=0.028), respectively, while other data was not statistically or significantly improved.

Conclusion : The MBSR program had some mild effects on the alleviation of distress and on the improvement of physiological status. However, this study did not show a reduced psychological status or quality of life for the metastatic breast cancer patient. For further research and practice, this study recommends an effective study design and an outcome analysis on both quantitative and qualitative aspects of the MBSR program. Also, future studies should consider implementing more beneficial sessions of MBSR for patients with advanced breast cancer.

PO08-05

DESCRIPTIVE STUDY ON PAIN AND MENOPAUSE SYMPTOMS OF BREAST CANCER PATIENTS WITH HORMONE THERAPY IN KOREA: SECONDARY ANALYSIS

Eunkyung Hwang[1*], **Myungsun Yi**[2]

[1] *Breast Care Center, Seoul National Univ. Hospital, Korea*
[2] *College of Nursing, Seoul National Univ., Korea*

Background/Purpose : In Republic of Korea, more than 100,000 women undergo breast cancer. Currently, about 70% of breast cancer patients are receiving hormone therapy, such as aromatase inhibitors. Although hormone therapy became a major treatment modality for breast cancer, its long-term side effects are not well explored. The most frequently reported side effect is pain and menopause symptoms. The purpose of the study was to identify and describe pain and menopause symptoms in breast cancer patients with hormone therapy.

Methods : The study was designed with a cross-sectional survey. The data were collected from 110 breast cancer women getting hormone therapy for more than 3 months. The participants were recruited in out-patient departments in a university hospital in Seoul during 2013. Pain was measured by Korean Version of Brief Pain Inventory and menopause symptom by Menopause Rating Scale.

Results : Most (88.2%) of the participants reported to have pain and 11.8% of them had a severe degree of pain. Almost (95.5%) of them had menopause symptoms and 60% of them had a severe degree of symptoms. Pain and menopause symptoms are strongly correlated each other ($p<0.005$). Pain was different by age ($R^2=0.82$, $\beta=0.300$), occupation, and economic status ($p<0.05$). Muscular-skeletal pain increased with aromatase inhibitor ($p<0.005$) and with age ($p<0.05$). And the rate of increasing pain due to hormone therapy was significantly higher in aromatase inhibitor group ($p=0.001$). Aromatase inhibitor significantly raised pain in the knee ($\chi^2=12.14$, $p=0.016$). Meanwhile, hot flush increased when they were young ($p<0.05$) or getting tamoxifen ($p<0.005$). Compliance with hormone therapy was different by the rate of increasing pain due to hormone therapy ($p=0.001$). Among the menopause symptoms, fatigue was the most frequently reported symptom (97.3%). And hot flush increased when they were young ($p<0.05$) or getting tamoxifen ($p<0.005$).

Conclusion : The results of the study indicate that interventions are needed for most breast cancer patients receiving hormone therapy to alleviate pain and menopause symptoms.

PO08-06

THE EFFECTS OF EXERCISE PROGRAM IN BREAST CANCER SURVIVORS: A META-ANALYSIS

Eun-Mi Kim[1], **Dong-Suk Lee**[2*]

[1] *Dept. of Nursing Science, Graduate School, Kangwon National Univ., Korea*
[2] *Dept. of Nursing, College of Medicine, Kangwon National Univ., Korea*

Background/Purpose : The aim of this study was to determine the effects of exercise program on physical and psychosocial outcomes in breast cancer survivors by systemic review and meta-analysis. It should be to provide basic data for oncology nursing practice and to suggest the exercise guideline for breast cancer survivors.

Methods : A total of 121 of articles have been identified through RISS database searching and 64 additional articles through Nanet, KISS (Koreanstudies Information Service System) and DBpia database searching. Keyword for searching was 'breast cancer & exercise' and finally 13 studies were included in meta-analysis. Used software was CMA (Comprehensive Meta-Analysis) version 2.0 and effect size was calculated by standardized mean difference (SMD) Hedge's g. Effect size was interpreted according to criteria of Cohen (1988).

Results : There were 2 studies of randomized control-group pre-post test design, 9 studies of nonequivalent control group pre-post test design and 2 studies of nonequivalent control group nonsynchronized design studies from 2000 to 2012 in Korea. The kind of exercise program were upper body stretching, shoulder muscle strength, Yoga, Thi chi etc. for early upper-limbs treatment, rehabilitation, change of body composition and improvement of muscle to strength during 2-12 weeks. A major field of these studies was physical education (8 studies), nursing science (3 studies), rehabilitation medicine (a single study) and physical therapy (a single study). The results of meta-analysis were as follows: First, exercise program showed 'large effect' on waist-to-hip ratio (1.051), total cholesterol (0.818), shoulder joint function test (1.170) and ROM of shoulder (flexion 0.932, extension 0.934, abduction 0.960). Secondly, it showed 'medium effect' on triglyceride (0.532), HDL-cholesterol (0.541), NK-cell of immunity (0.630) and quality of life (0.649). Lastly, It showed 'small effect' on internal rotation (0.349) and external rotation (0.377). But lean body mass, rate of body fat, body mass index, grip strength and upper limbs edema were not statistically significant. In addition, Psychosocial outcome in this study was selected as only quality of life since pain and other considered psychosocial outcomes had been not reported mean and standard deviation and couldn't calculate effect size.

Conclusion : This study showed exercise program was effective in various physical and psychosocial outcomes in breast cancer survivors. But lean body mass, rate of body fat, body mass index, grip strength and upper limbs edema, which were not effective statistically, need to be re-constructed in aspect of period because 2-12 weeks were quite short time to change.

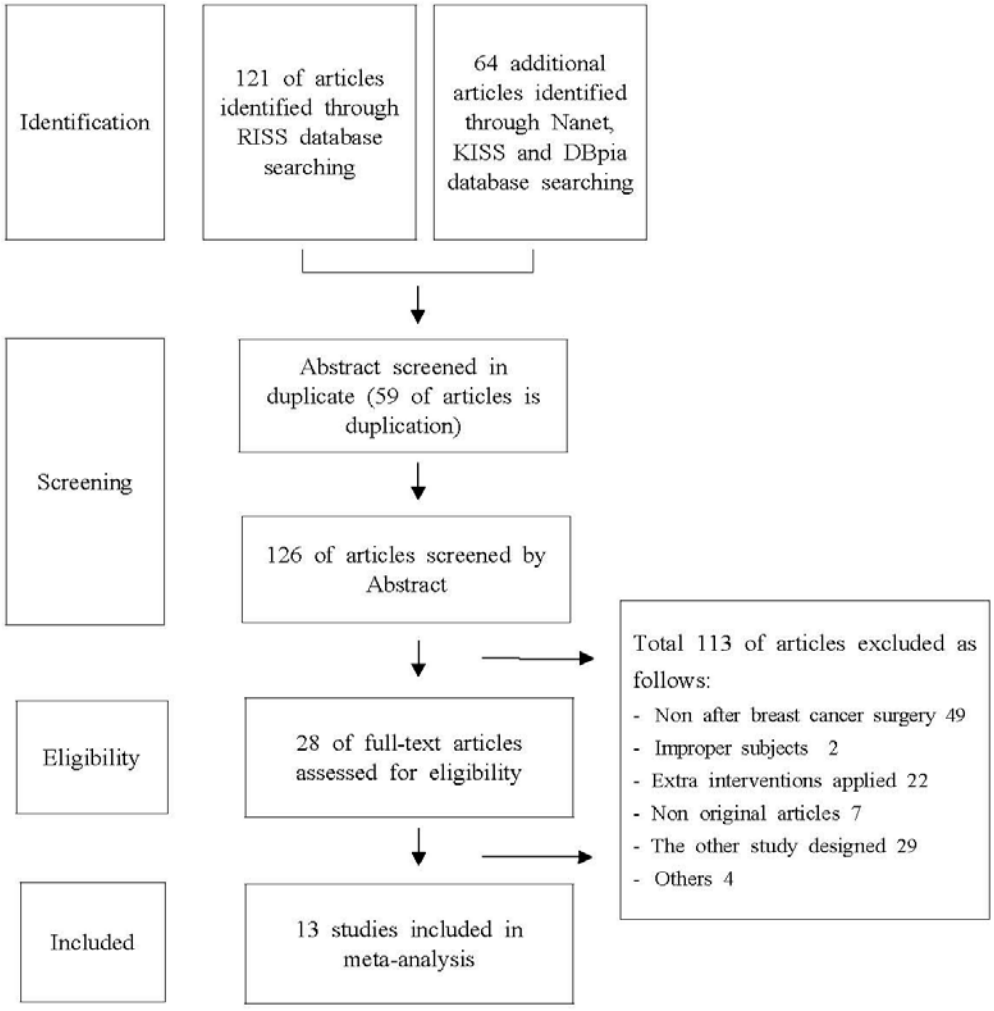

Figure 1. Study flow diagram

PO08-07

EFFICACY OF A WEB-BASED SELF-MANAGEMENT EXERCISE AND DIET INTERVENTION PROGRAM WITH TAILORED MOTIVATION AND ACTION PLANNING FOR BREAST CANCER SURVIVORS: A RANDOMIZED CONTROLLED TRIAL

Myung Kyung Lee[1], **Young Ho Yun**[2*], **Hyeoun-Ae Park**[3], **Eun Sook Lee**[4], **Kyung Hae Jung**[5], **Dong-Young Noh**[6]

[1] *Dept. of Nursing, Dong-A Univ., Korea*
[2] *Hospital and College of Medicine, Cancer Research Institute, Seoul National Univ., Korea*
[3] *College of Nursing, Seoul National Univ., Korea*
[4] *Center for Breast Cancer, National Cancer Center, Korea*
[5] *Dept. of Oncology, College of Medicine, Univ. of Ulsan, ASAN Medical Center, Korea*
[6] *Dept.of Surgery, College of Medicine, Cancer Research Institute, Seoul National Univ., Korea*

Background/Purpose : The aim of the study was to determine whether a Web-based self-management diet and exercise program was effective for breast cancer patient not practicing diet and exercise behaviors.

Methods : Participants were randomly assigned either to Web-based, tailored self-management exercise and diet program featuring the delivery of education, the development of the capacity to plan, and automatic feedback employing transtheoretical model-based strategies or to the attention control group, which used booklets. We measured behaviors practiced at the goal level, dietary consumption, and moderate-intensity exercise as primary outcome, and health-related quality of life (HRQOL), anxiety, depression, and fatigue as secondary outcome at the baseline and 12 weeks.

Results : Fifty-nine breast cancer patients who had completed curative surgery and primary cancer treatment were recruited. Compared with the control group, the intervention group had an improvement in number practiced at least two of the three behavioral domains at 12 weeks (18.8 % of patients in the control group, 66 percent of patients in the intervention group) ($p=0.0002$). The proportion of moderate-intensity aerobic exercise for at least 150 minutes per week ($p<0.0001$) and eating five servings of fruit and vegetables per day ($p=0.001$) increased to a greater extent in the intervention group than in controls. The intervention group also showed a greater improvement in overall diet quality ($p=0.001$) and motivational readiness for exercise ($p<0.0001$) than did controls.

Conclusion : Health Planner can be effective in improving the capacity of self-management related to diet and exercise behaviors and promoting lifestyle changes in breast cancer patients.

PO08-08

RELATIONSHIPS BETWEEN LIFESTYLE BEHAVIORS AND HEALTH-RELATED QUALITY OF LIFE AMONG BREAST CANCER SURVIVORS

Soo Hyun Kim[1], **Youngkyu Song**[2]

[1] *Dept. of Nursing, Inha Univ., Korea*
[2] *Graduate School, The Catholic Univ. of Korea, Korea*

Background/Purpose : The purpose of this study was to examine the levels of physical activity (PA), exercise habit, and diet quality and identify associations with health-related quality of life (HRQOL) outcomes among breast cancer survivors.

Methods : This study was a cross-sectional descriptive study design. A total of 132 women (mean age = 50.3 years) with breast cancer having completed their therapy were recruited at one university-based cancer center in Korea. Subjects completed a self-reported questionnaire, including the International Physical Activity Questionnaire - short form (IPAQ-SF), Mini Dietary Assessment (MDA), European Organization of Research and Treatment of Cancer Quality of Life questionnaire Core 30 items (EORTC QLQ-C30), and Hospital Anxiety and Depression Scale (HADS). For analysis, Three lifestyle behaviors were categorized as dichotomous variable as follows; IPAQ-SF, moderate to high physical activity versus low; exercise habit, as more than 150 minutes per week versus or less; and diet quality, more than MDA median scores versus less. Thus, there are four possible mutually exclusive lifestyle behavior clusters (i.e. group 1, meeting no healthy lifestyle; group 2, meeting only one healthy lifestyle; group 3, meeting any two healthy lifestyles, and group 3, meeting all three healthy lifestyles).

Results : According to the IPAQ-SF classification, 29.5% of the participants had low physical activity, 46.2% had moderate physical activity, and 24.2% had high physical activity. Most women (72.0%) were participating in a regular exercise over the past year and almost all (84.2%) met the public recommendation for exercise (i.e., more than 150 minutes per week). The total MDA median scores were 42.0 (possible range, 10 to 50). In terms of lifestyle behavior clusters, 32.5% women were meeting all three healthy lifestyle behaviors, 57.6% were meeting one or two behaviors, and 10.6% were not meeting any behavior. Analyses of covariance showed that there were significant differences in HRQOL outcomes among four groups. Women who were meeting all three lifestyle behaviors (group 4) showed significantly better scores in global QOL, anxiety, and depression than other groups. Women who were not meeting any behavior (group 1) showed significantly lower scores in physical function, emotional function, global QOL, anxiety, depression than other groups.

Conclusion : The association between the healthy lifestyle and HRQOL in breast cancer survivors appears to be cumulative. Interventions to increase physical activity, encourage a regular exercise and improve diet quality are warranted and may have additive effects on the HRQOL of breast cancer survivors.

PO08-09

HUSBANDS' CARING EXPERIENCES FOR WOMEN WITH BREAST CANCER IN KOREA

Eun Jin Kwon

Graduate School of Nursing, Seoul National Univ., Korea

Background/Purpose : The purpose of the study was to describe the caring experiences of husbands for women with breast cancer in Korea.

Methods : The data were collected by individual in-depth interviews with seven participants during 2010-2012. Transcribed data were analyzed using Colaizzi's phenomenological analysis.

Results : A total of 10 theme clusters were derived from the analysis: Hidden fear of world without wife; Responsibility with guilt for breast cancer; Desperate search for treatment information; Becoming active companion of treatment itinerary; Comfort for wife's hair loss with sympathy; Multitasks undertaken at one time; Gain and loss by coming out publically; Wife-oriented open communication; New alternative sexual life; Everyday life matured by hardship.

Conclusion : The results of the study can help oncology professionals in developing couple counseling programs by providing insights of the husbands' experiences of caring for women with breast cancer.

PO08-10

CHILDREN'S EXPERIENCES WITH THEIR MOTHER'S BREAST CANCER: 'FINDING MYSELF IN CHAOS'

Miyoung Park[1], **Juhye Jin**[2*], **Hee Soon Kim**[3], **Il Sun Ko**[3], **Sue Kim**[3]

[1] *Dept. of Nursing, Gangneung Yeongdong College, Korea*
[2] *Dept. of Nursing, Univ. of Ulsan, Korea*
[3] *Dept. of Nursing, College of Nursing, Yonsei Univ., Korea*

Background/Purpose : Little research has investigated on how children whose mothers were diagnosed with breast cancer experience their mothers' disease. The purpose of this qualitative study that was based on grounded theory was to explore the experiences of children whose mothers had breast cancer.

Methods : Data were obtained for 1 year from June 2012 to June 2013, and collected through face-to-face in-depth interviews using an interview guide that consisted of both semi-structured and open questions. Interviews were conducted in participants' homes or the researcher's office. The age of participants ranged from 11 to 18 (n=12). Each interview lasted 30 to 120 minutes, and the number of interviews varied from one to three per participant. Data collection and analysis were conducted simultaneously, and constant comparative methods were used. Based on the work of Strauss and Corbin (1998), 3-level-coding (open, axial, and selective) was used to conceptualize data. The researcher also used diagramming as an additional analysis strategy to identify relationships among concepts and clarify various situations. Field notes from interviews and memo-writing were integrated into the analytic process.

Results : Twelve major conceptual categories resulted from the coding process and included the following: accessing bad news, cognizing severity, involving into emotional confusion, watching sick mother, experiencing family change, searching on breast cancer, replacing the role of mother, deciding to do 'HYO', avoiding the situation, overcoming the situation, being flat (blunt), and feeling growing-up. The core category of finding myself in chaos was drawn from a series of processes of hearing the news on mother's breast cancer, being emotionally confused, watching mother's struggle with breast cancer, doing 'HYO' for sick mother, and finding myself. Participants' experiences began with hearing about their mothers' breast cancer or having inkling and the emotional confusion that followed. How severely cognizing the cancer and the current relationship between mother and child also affected the participants' emotional turmoil. With various emotions and feelings, participants were involved in their mothers' battles with breast cancer. While directly and indirectly experiencing the mothers' cancer treatment, participants tried to deal with their emotions; one way they did this was searching for information on breast cancer and taking on their mothers' roles. Gradually, participants tried to find how to best help their sick mothers, and consequently they did 'HYO'. Participants also tried to overcome stressful situations that resulted from their mothers' illnesses. They also sometimes avoided the situation. Throughout the period of emotional confusion, such as chaos, participants regarded themselves as being mature or calm. The consequences of either growing-up or being blunt were found within the process of making the effort to finding 'self.'

PO08-10

Conclusion : The experiences of children whose mothers have breast cancer were the products of actions and interactions among human beings at the level of the child participant, his or her family, and society or culture, including the individual and his or her family. Within the three levels of dimensions, participants who were school-aged or teenagers tried to find themselves for their sick mother, in spite of their struggle with various emotions and feelings. The resulting conceptualization of 'finding myself in chaos' can help nurses provide extended quality of care for patients with breast cancer and their children, especially in terms of bettering understanding children's emotional struggles and intervening in their subsequent behaviors as possible.

PO08-11

THE RELATIONSHIP AMONG UNCERTAINTY, BODY IMAGE, SOCIAL SUPPORT AND QOL OF YOUNG BREAST CANCER SURVIVORS

Jihye Kim[1*], Sue Kim[2], Hyangkyu Lee[2], Soo Hyun Kim[3]

[1] *Dept. of Oncology Nursing, ASAN Medical Center, Korea*
[2] *Dept. of Clinical Nursing, College of Nursing, Yonsei Univ., Nursing Policy Research Institute, Korea*
[3] *Dept. of Nursing, Inha Univ., Korea*

Background/Purpose : Breast cancer is the second most common cancer in women in Korea and especially more prevalent in women 35 years of age and younger than other countries. Many prior surveys investigated physical and psychosocial problems of breast cancer survivors. However, there is a lack of research on young breast cancer survivors' psychosocial issues such as dating, marriage, childbirth, academic performance, and employment. This descriptive survey aimed to investigate the relationship among uncertainty, body image, social support, and quality of life of young breast cancer survivors aged 35 years or younger.

Methods : Data were collected from women 35 years of age and younger diagnosed with breast cancer recruited from a Young Breast Cancer Clinic, oncology outpatient clinic, and breast and endocrine surgery outpatient clinic of 'A' hospital in Seoul. The study is in progress, and informed written consent was obtained from all participants (30 out of a target of 60). The survey questionnaires consisted of Mishel's Uncertainty in Illness Scale (1981), a body image tool (Jun, 1996), Perceived Social Support Scale (Blumenthal, 1988), and the Quality of Life (QOL)-Cancer Survivorship Scale (Ferrell & Dow, 1995) to determine quality of life.

Results : Findings from preliminary analysis are as follows Table 1. The relationships between Body image and QOL showed a higher correlation. The relationships between Uncertainty and QOL showed a moderate correlation. The data will be analyzed with descriptive statistics, t-test, one-way ANOVA, and Pearson's correlation using SPSS 18.0 program.

Conclusion : The results of this survey indicate that the Korean young breast cancer survivors are in need of help especially in the psychosocial issues. Additionally, this survey will be used to get basic data for young breast cancer survivors' education program. Therefore, medical team including nurses should support young breast cancer survivors by providing counseling and education to improve their quality of life.

PO08-11

Table 1

The Relationship among Uncertainty, Body image, Social support and Quality of life Of Young breast cancer survivors (N=30)

Variable	Quality of life		
	Pearson's correlation	*r*	*p*
Uncertainty [a]		.489**	.006
Uncertainty [b]		.523**	.003
Body image		-.782**	.000
Social support		.308	.098

Note. * p < 0.05, ** p < 0.01

Uncertainty [a]: The variable used 21 questionnaires consisted of Mishel's Uncertainty in Illness Scale (1981).

Uncertainty [b]: The variable used 5 questionnaires be consulted one professor of college of nursing about young breast cancer survivors' characteristics.

Table 1

PO08-12

EMOTIONAL DISTRESS IN NEWLY DIAGNOSED PATIENTS WITH BREAST CANCER: ITS ASSOCIATIONS WITH DEMOGRAPHIC, CLINICAL AND COPING VARIABLES

Soo Hyun Kim[1], **Young Up Cho**[2], **Sei Joong Kim**[2], **Mi Sook Han**[3]

[1] *Dept. of Nursing, Inha Univ., Korea*
[2] *Dept. of Breast and Endocrine Surgery, Inha Univ. Hospital, Korea*
[3] *Dept. of Nursing, Inha Univ. Hospital, Korea*

Background/Purpose : This study examined the levels of emotional distress and its associations with demographic, clinical, and coping variables among newly diagnosed patients with breast cancer.

Methods : A total of 101 newly diagnosed patients with breast cancer (mean age=51.2 years) were recruited from a comprehensive hospital in Korea. Subjects completed a self-reported measurement, which included the Mini-Mental Adjustment to Cancer (Mini-MAC) and Hospital Anxiety and Depression Scale.

Results : According to the results, 12.9% and 8.9% of subjects showed clinical anxiety and depression, respectively. Younger women, living with a partner, and higher education showed an association with higher anxiety at time of diagnosis. Regarding coping variables, significant differences in helpless-hopeless, anxious precaution, and fighting spirit were observed between the non- anxiety group and the anxiety group. Younger women, premenopausal, and higher education showed an association with higher depression. Regarding coping variables, significant differences in all subscales of Mini-MAC, except for cognitive avoidance, were observed between the non-depression group and the depression group. In the regression analysis of anxiety, anxious precaution and helpless-hopeless coping style and marital status were significant determinants (R^2 =0.563, F=43.596, p<0.001), while anxious precaution and fighting spirit coping style were significant determinants of depression among newly diagnosed patients with breast cancer (R^2 =0.339, F=26.383, p<0.001).

Conclusion : Findings of our study indicate that anxiety is more common at diagnostic phase. Emotional distress in newly diagnosed patients with breast cancer was significantly influenced by coping style. Therefore, psychosocial interventions to increase adaptive mental coping strategy in order to ameliorate emotional distress are needed.

PO08-13

SPIRITUAL HEALTH AND FATIGUE OF PATIENTS WITH BREAST CANCER ACCORDING TO TREATMENT PHASES

Young Sook Tae[1], **Gum Hee Choi**[2], **Suhye Kwon**[1]

[1] *College of Nursing, Kosin Univ., Korea*
[2] *Dept. of Nursing, St. Mary's Hospital, Korea*

Background/Purpose : The study was to identify the level of spiritual health(hope, comfort, self-esteem, trust) and fatigue in women with breast cancer according to three treatment phases (post op phase, adjuvant phase, follow up phase).

Methods : The research method was a cross-sectional descriptive study. Data were collected from 161 women patients with a diagnosis of breast cancer. Both in-patient and out-patient units from two general hospitals were the source of subjects. The subjects completed two standardized instruments: the 'Spiritual Health Scale' developed by Highfield and the 'Fatigue Scale' developed and revised by Piper. The data were analyzed using frequency, percentage, χ^2, ANOVA, Sheffe's test, Pearson's correlation coefficients, and Multiple regressions.

Results : The subscale scores of self-esteem of spiritual health and fatigue in patients with breast cancer differed among the three treatment phases ($F=3.14$, $p=0.046$; $F=3.31$, $p=0.039$). Significant correlations were found between spiritual health and fatigue. The variables which explained 29% of the variance in fatigue in breast cancer patients were education, religious belief, economic status, and spiritual health.

Conclusion : The study results demonstrated that spiritual health significantly explain fatigue. It is needed to develop nursing interventions to improve the spiritual health of breast cancer patients to manage fatigue according to treatment phases.

PO08-13

Table 1. Spiritual Health and Fatigue by Each Treatment Phases

(N=161)

Variables	Range	Post Op (n=52) Mean(SD)	Adjuvant Tx (n=55) Mean(SD)	Follow Up (n=54) Mean(SD)	F	p	Sheffe
Spiritual health	66 - 145	111.85(18.40)	110.51(17.44)	107.98(19.03)	0.62	.534	
Hope	5 - 25	18.71(5.36)	18.22(4.50)	18.30(5.36)	0.14	.873	
Comfort	18 - 49	35.33(6.69)	36.58(7.04)	35.72(6.51)	0.49	.616	
Self-esteem	20 - 52	40.04(6.92)[a]	38.29(7.62)[b]	36.48(7.35)[c]	3.14	.046	a>c
Trust	8 - 24	17.77(2.80)	17.42(3.19)	17.48(2.64)	0.22	.801	
Fatigue	19 - 175	77.94(36.64)[a]	93.53(39.10)[b]	77.00(37.02)[c]	3.31	.039	b>a, c

Post Op= post operation phase; Adjuvant Tx=adjuvant treatment phase

Follow Up=follow-up phase

Table 1

Table 2. Multiple Regression for Predictors of Fatigue

(N= 161)

Independent variables	step 1					step2				
	B	SE	β	t	p	B	SE	β	t	p
Education	-20.94	6.63	-.27	-3.16	.002	-14.09	-6.21	-.18	-0.18	.025
Religious belief	4.42	2.23	.15	1.98	.049	-1.17	2.28	-.04	-0.51	.609
Economic status	-9.43	3.88	-.19	-2.43	.016	-3.60	3.71	-.07	-0.97	.332
Spiritual health						-0.98	0.18	-.47	-5.54	<.001
R^2	.15					.29				
Adjusted R^2	.13					.27				
F	7.11(< .001)					12.90(< .001)				

Independent variables: Education, Religious belief, Economic status, Fatigue

Dependent variable: Fatigue

Table 2

PO08-15

THE INFLUENCE OF HOPE, RESILIENCE, AND SPOUSAL SUPPORT ON QUALITY OF LIFE IN WOMEN WITH BREAST CANCER

Young Mi Ryu*, Myungsun Yi

College of Nursing, Seoul National Univ., Korea

Background/Purpose : The incidence rate of breast cancer has increased rapidly during the past decades. Breast cancer is a disease affecting all aspects of one's life and psychosocial area is one of the most affecting areas. Thus oncology nurses pay attention to improve quality of life of women with breast cancer by focusing on psychological and social aspects in addition to their physical aspect. Resilience is known to be an important variable in overcoming adversity and to adjust positively to cancer, as well as hope and spousal support. This study was designed to identify the influence of hope, resilience, spousal support on quality of life in women with breast cancer in Korea.

Methods : A predictive correlational design was used. The data were collected by questionnaires from a convenience sample of 163 women with breast cancer in 2012. The data were analyzed using descriptive statistics, t-test, ANOVA, Pearson's correlation coefficients, and stepwise multiple regression.

Results : Mean age of the participants was 51.47 (SD=6.39) and 46% reported to have stage II at diagnosis and 59.5% had less than 5 years since diagnosis. The quality of life was different by age and type of surgery. Hope, resilience, spousal support, and quality of life were significantly correlated each other ($r=0.160$-0.640, $p<0.05$). Quality of life was accounted for 23.4% of the variance by resilience, spousal support, and type of surgery. The most affecting factor was resilience, which explained 18.9% of the variation.

Conclusion : The results of the study show the importance of resilience in explaining the quality of life in Korean women with breast cancer. Thus, oncology nurses should integrate resilience to develop and implement more effective interventions to improve their quality of life.

PO08-16

PATTERNS OF HEALTH-RELATED QUALITY OF LIFE FROM DIAGNOSIS TO 24 MONTHS AFTER COMPLETION OF ACTIVE TREATMENT

Eun-Kyung Choi[1], Im-Ryung Kim[1], Danbee Kang[2], Soo Jung Park[2], Seok-Jin Nam[3], Jeong Eon Lee[3], Se-Kyung Lee[3], Dong-Young Noh[4], Wonshik Han[4], Juhee Cho[5*]

[1] *School of Medicine, Sungkyunkwan Univ., Cancer Education Center, Samsung Comprehensive Cancer Center, Samsung Medical Center, Korea*
[2] *Dept. of Health Science and Technology, SAHIST, Sungkyunkwan Univ., Korea*
[3] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*
[4] *Dept. of Surgery, School of Medicine, Seoul National Univ., Seoul National Univ. Hospital, Korea*
[5] *Dept. of Health Sciences and Technology, School of Medicine, Sungkyunkwan Univ., Cancer Education Center, Samsung Comprehensive Cancer Center, Samsung Medical Center, Korea*

Background/Purpose : Breast cancer patients experience various adverse effects of cancer treatment even years after completion of therapy. This not only affect patients' functional and physical well-being considerably but also on progression of the disease and survival. This study evaluated health-related quality of life in breast cancer patients from the time of diagnosis to the 24 months after completion of active treatment.

Methods : Between July 2010 and July 2011, we recruited patients with non-metastatic breast cancer who were expected to receive adjuvant breast cancer treatments (n=432) from two (different) cancer hospitals in Seoul, Korea. With help from a trained interviewer, study participants completed questionnaires on health-related quality of life at enrollment (before surgery), 2 weeks, 3 months, 6 months, 12 months, and 24 months after surgery. Health-related quality of life was assessed using EORTC-QLQ-C30 and QLQ-BR23. Socio-demographic and clinical characteristics were also assessed. To examine changes overtime, mixed effect analysis was performed using STATA 12.

Results : After excluding 8 patients with recurrence during follow-up, the final sample was consisted with 424 patients. The mean age of the participants was 46.4 (SD 7.91) years. 87.6% of participants were married, and 46.1% and 36.8% of them had stage I and II breast cancer, respectively. 82.7% of the patients had lumpectomy, and 72.4%, 85.9% and 63.7% had chemotherapy, radiotherapy and hormone therapy, respectively. Comparing to the baseline, global health status, and quality of life, emotional and social functional slightly increased over time. In contrast, patients reported worse physical, role and cognitive function and these symptoms continued to be persistent at 24 months follow-up ($p<0.001$). Fatigue, insomnia, constipation and diarrhea were as the most disturbing treatment related symptoms at re-entry periods ($p<0.001$). Although there were deteriorations in patients' scores for body image during follow-up time, breast cancer patients keep having problems with low body image even after 24 months post-surgery. Symptoms in breast and arm worsened after surgery and then improved throughout the time but they never reached the baseline level.

Conclusion : Breast cancer patients reported problems with functioning and physical symptoms even after 24 months following their treatments, which did not return to the base-line. This persistent low quality of life would indicate further needs in health care and psychosocial support for breast cancer patients during follow-up care after completion of the treatment.

PO08-17

COMPARISONS OF PERCEIVED CLINICAL DECISION-MAKING ISSUES BETWEEN CANCER PATIENTS

Ae Ran Park[1], **Hyang Sook So**[2], **Myeong Jeong Chae**[3]

[1] *Dept. of Nursing in Graduate School, Chonnam National Univ., Korea*
[2] *College of Nursing, Chonnam National Univ., Korea*
[3] *Dept. of Nursing, Gwangju Woman's Univ., Korea*

Background/Purpose : The purpose of this study is to identify the person who make decision at clinical decision-making situation and to identify the differences of opinions of the advanced directives (living wills, etc.) and its legalization between patient, family, medical staffs in oncological nursing units. There are diverse clinical decision-making attitudes according to various family system or size. After the year of 2010, a single person household is rapidly growing and the first order of size of a family in Korea. Person, esp. young people who lives alone show a tendency to place his or her own on priority to make decisions because self-own is an independent person with fundamental human rights.

Methods : A total of two hundred people who are cancer patients, their family, physicians, and nurses were recruited from a regional national cancer center. The structured questionnaires were consisted with 23 items, which selected from domestic and foreign literature review. The collected data were analyzed by descriptive statistics using SPSS 19.0 version.

Results : The subjects of this study were cancer patients and their family about forty and fifty, and physicians and nurses about twenty and thirty, respectively. About two third of patients and family were married about half of the medical staffs were unmarried. Around sixty percent of the patients and their family were religious and medical staffs were fifty percent. About half of them have experienced the bioethics-related education or seminars. Patients wanted to know first their diagnosis, and responded person who made decision of treatment options would be physician first and then themselves. On the while, their family answered that decision-maker would be both of patient and family (χ^2=29.38, p<0.001; χ^2=31.05, p<0.001). At several situations, patients' attitude about making decisions is different from the one of their family. On the other hand, person who would be discussed and made decisions about supportive care in recovery period after discharge from hospital was patient's own and their family (χ^2=24.57, p<0.001)(Table 1). Physicians and nurses who have not the experience about life sustaining treatment were over seventy to eighty percent (χ^2=11.38, p=0.010). Physicians who didn't aware the advanced directive were over thirty percent, and in case of patients and family were increased at twice the rate of them (χ^2=19.51, p<0.001). The rates of positive answer about ethical justification and need for legalization of advanced directives was over seventy to ninety percent in all four groups. Lastly, the rate of positive answer about making attempt of advanced directives after legalization was over eighty percent, and the use of living will among advanced directives was over sixty percent in all four groups (Table 2).

PO08-17

Conclusion : We have to put emphasis on the patient's autonomy & self-determination in critical situations clinically. At several situations, patients' attitudes about making decisions are different from the one of their family. In order to be provided the supportive care from significant others, esp. family, cancer patients want to discuss and select the options with their family. At this point, our society would be required to held the public opinion of the Advanced Directive actively and should be established a national legislation of A.D.(Advanced Directive).

<Table 1> Whereabout of clinical decision-making about medical care

(N=200)

Variables		Patient	Family	Physician	Nurse	x^2-test (p)
		No (%)	No (%)	No (%)	No (%)	
Person who will be informed of cancer diagnosis first	cancer patient	21 (42.0)	7 (14.0)	8 (16.0)	11 (22.0)	29.38 (<.001)
	family member	9 (18.0)	22 (44.0)	26 (52.0)	9 (18.0)	
	patient & family member	20 (40.0)	21 (42.0)	16 (32.0)	30 (60.0)	
Decision-maker about treatment options	patient	16 (32.0)	11 (22.0)	16 (32.0)	18 (36.0)	31.05 (<.001)
	patient & family member	15 (30.0)	25 (50.0)	27 (57.0)	28 (56.0)	
	physician	17 (34.0)	8 (16.0)	3 (6.0)	-	
	family member	2 (4.0)	6 (12.0)	4 (8.0)	4 (8.0)	
Final decision-maker about critical options	cancer patient	37 (74.0)	32 (64.0)	42 (84.0)	46 (92.0)	5.98 (.112)
	family member	7 (14.0)	12 (24.0)	6 (12.0)	3 (6.0)	
	physician	6 (12.0)	6 (12.0)	2 (4.0)	1 (2.0)	
Decision-maker about where to go after discharge	cancer patient	24 (48.0)	14 (28.0)	9 (18.0)	13 (26.0)	24.57 (<.001)
	family member	5 (10.0)	8 (16.0)	20 (40.0)	7 (14.0)	
	patient & family member	21 (42.0)	28 (56.0))	21 (42.0)	30 (60.0)	
Decision-maker about primary care-giver after discharge	cancer patient	13 (26.0)	10 (20.0)	2 (4.0)	4 (8.0)	15.26 (.018)
	family member	17 (34.0)	18 (36.0)	24 (48.0)	16 (32.0)	
	patient & family member	20 (40.0)	22 (44.0)	24 (48.0)	30 (60.0)	

Table 1

PO08-17

<Table 2> Advanced Directives-Related Issues

(N=200)

Variables		Patient No (%)	Family No (%)	Physician No (%)	Nurse No (%)	x^2-test (p)
Experience about Life Sustaining Treatment	Have	6 (12.0)	4 (8.0)	16 (32.0)	10 (20.0)	11.38 (.010)
	Have not	44 (88.0)	46 (92.0)	34 (68.0)	40 (80.0)	
Degree of Recognition about Life Sustaining Treatment	Unkown	13 (26.0)	11 (22.0)	1 (2.0)	5 (10.0)	14.28 (.003)
	Somewhat	35 (70.0)	35 (70.0)	27 (54.0)	32 (64.0)	
	Considerably	2 (4.0)	4 (8.0)	22 (44.0)	13 (26.0)	
Awareness of Advanced Directive	Yes	22 (44.0)	16 (32.0)	34 (68.0)	34 (68.0)	19.51 (<.001)
	No	28 (56.0)	34 (68.0)	16 (32.0)	16 (32.0)	
Ethical Justification of Advanced Directive	Yes	38 (76.0)	38 (76.0)	44 (88.0)	44 (88.0)	4.88 (.181)
	No	12 (24.0)	12 (24.0)	6 (12.0)	6 (12.0)	
Need for Legalization of Advanced Directive	Yes	43 (86.0)	42 (84.0)	47 (94.0)	45 (90.0)	2.90 (.408)
	No	7 (14.0)	8 (16.0)	3 (6.0)	5 (10.0)	
Use of Advanced Directive, When Legalized	Yes	40 (80.0)	41 (82.0)	42 (84.0)	44 (88.0)	1.27 (.736)
	No	10 (20.0)	9 (18.0)	8 (16.0)	6 (12.0)	
Intention to Designate Living Will or Durable Power of Attorney	Living will	30 (60.0)	36 (72.0)	30 (60.0)	32 (64.0)	4.00 (.677)
	Durable power of Attorney	7 (14.0)	2 (4.0)	7 (14.0)	5 (10.0)	
	Both of them	13 (26.0)	12 (24.0)	13 (26.0)	13 (26.0)	
Legislation on Family Claims	Necessary	47 (94.0)	48 (96.0)	45 (90.0)	47 (94.0)	1.56 (.668)
	Unnecessary	3 (6.0)	2 (4.0)	5 (10.0)	3 (6.0)	

Table 2

PO08-18

SATISFACTION SURVEY ON BREAST SELF-EXAMINATION EDUCATION

Mi Ae Chang

Dept. of Surgery, ASAN Medical Center, Korea

Background/Purpose : It is vital to apprehend the correct breast self-examination method, early detection and prevent breast cancer through educational programs.

Methods : The breast self-examination program was operated between October 2011 to May 2012, on a monthly basis on breast cancer patients and the general public through lectures and practical training using breast model. Twenty one people who participated in the education and training gave their evaluation through the self-questionnaire (5-point scale).

Results : The distribution of participants follows: fifty six per cent of survey respondents were patients, 31% were caregivers; by age, respondents in their 50s were the majority at 38%; by gender, 19% were men and 81% were women; by education, more than 81% received high school education level. The overall satisfaction survey resulted that 55% were very satisfied, 35% were satisfied. In the case of the process of the program satisfaction resulted that 73.7% were very satisfied and 15.8% were satisfied. With regards to how much this training help with the respondents, 68.4% answered that it was very helpful and 21.1% said it was helpful. With regards to the comfort of the educational environment, 52.6% strongly agreed and 6.3% answered with a yes. For future participation on the re-survey, 95% agreed to do so, in which 40% strongly agreed to participate. In addition, 57.9% will be strongly recommended to others and 36.8% will recommend to others.

Conclusion : Most patients have heard of the breast self-examination but the majority did not know how to carry it out. Education through using breast model increased the understanding and early detection of breast cancer. Through educational programs, future research is needed to investigate how well the breast self-examination has been implemented.

PO08-19

FACTORS AFFECTING SYMPTOM CLUSTERS IN PATIENTS WITH BREAST CANCER RECEIVING CHEMOTHERAPY

Seonmi Cho[1], **Ilsun Ko**[2*], **Sue Kim**[2], **Jeongyoon Song**[3], **Sunyoung Min**[4]

[1] *College of Nursing, Yonsei Univ. Hospital, Korea*
[2] *College of Nursing, Yonsei Univ., Korea*
[3] *Dept. of Surgery, College of Medicine, Gangdong Kyunghee Univ., Korea*
[4] *Dept. of Surgery, College of Medicine, Kyunghee Univ., Korea*

Background/Purpose : Cancer patients commonly experience various symptoms simultaneously during receiving chemotherapy and various symptoms experienced simultaneously by the cancer patient are called 'symptom cluster', which amplify another subsidiary symptoms. The purpose of this study was to identify factors that influence symptom clusters dividing two aspects of frequency and intensity in patients with breast cancer receiving chemotherapy for developing multidimensional intervention.

Methods : This study was a descriptive study. Participants in this study were 79 women with diagnosed staged I~IV breast cancer, scheduled to receive adjuvant or neoadjuvant chemotherapy. The structured questionnaire used for this study included sub-scales of EORTC QLQ-C30 & EORTC QLQ-BR23 for measuring frequency and intensity of physical and emotional symptoms, the QSC-R23 for measuring psychological distress and questionnaire for measuring support of family and health care providers developed by Tae, Yong Sook. Data were collected from April 20 to November 30, 2012 and analyzed using t-test, ANOVA, Pearsons' correlation's coefficient, factor analyses and multiple regressions.

Results : Symptoms were classified to three clusters in aspect of frequency; an emotional disturbance cluster(loss of memory-depression-petulance-constipation- nervousness - dyspnea), pain cluster(pain of breast, pain of arm/shoulder, nausea, pain of whole body) and fatigue cluster(fatigue-sleep disorders-loss of appetite-difficulty concentrating) and four clusters in aspect of intensity; a fatigue cluster (fatigue-loss of appetite-nausea-sleep disorders), emotional disturbance cluster (nervousness-petulance-depression), cognitive impairment cluster (loss of memory-difficulty concentrating-dyspnea-constipation) and pain cluster(pain of arm/shoulder-pain of whole body-pain of breast). Both frequency and intensity of symptom clusters were significantly influenced by the psychological distress, several disease related factors (performance of surgery, the past treatment, cancer metastasis, place in treatment), and demographic factors (age, family members). Situational factors such as family and health care givers' supports were not significantly related with both frequency and intensity of symptom clusters.

Conclusion : The symptom clusters of breast cancer patients receiving chemotherapy were classified to three clusters in aspect of frequency and four clusters in aspect of intensity. Psycho-social distress affected to all symptom clusters in aspects of frequency and intensity. For establishing effective management of physical and emotional symptoms of the breast cancer patients receiving chemotherapy, it is needed to identify frequency and intensity of symptom clusters and to decrease their psycho-social distress.

PO08-19

Figure1. Factor analysis according to participants' symptom frequency. (N=79)

	Factor1	Factor2	Factor3	Factor4	Naming
Loss of memory	.787				Emotional
Depression	.758				Disturbance
Petulance	.723				Cluster
Constipation	.651				
Nervousness	.646				
Dyspnea	.511				
Pain of breast		.767			Pain
Pain of arm/shoulder		.712			Cluster
Nausea		.611			
Pain of whole body		.530			
Fatigue			.754		Fatigue
Sleep disturbance			.688		Cluster
Loss of appetite			.598		
Difficulty concentrating			.564		
Diarrhea				.841	-
Eigen value	5.665	1.527	1.313	1.153	
Variance explained,%	22.792	16.269	15.989	9.335	
Total variance explained, %			55.050	54.385	
Internal consistency (cronbach's a)	.855	.714	.714	-	

Figure 1

Figure2. Factor analysis according to participants' symptom intensity. (N=79)

	Factor1	Factor2	Factor3	Factor4	Factor5	Naming
Fatigue	.762					Fatigue
Loss of appetite	.697					Cluster
Nausea	.604					
Sleep disturbance	.603					
Nervousness		.836				Emotional
Petulance		.805				Disturbance
Depression		.774				Cluster
Loss of memory			.853			Cognitive
Difficulty concentrating			.631			Impairment
Dyspnea			.598			Cluster
Constipation			.590			
Pain of arm/shoulder				.850		Pain
Pain of whole body				.705		Cluster
Pain of breast				.588		
Diarrhea					.832	-
Eigen value	5.157	1.622	1.443	1.226	1.109	
Variance explained,%	16.068	15.907	15.028	13.331	10.043	
Total variance explained, %				60.334	70.377	
Internal consistency (cronbach's a)	.719	.833	.739	.709	-	

Figure 2

Figure3. Factors affecting the participants' symptom frequency cluster (N=79)

Factor	Cluster	B	b	t	p	R^2	Adj R^2	F
Psycho-social	Emotional disturbance cluster	,124	,589	6,701	,000	,365	,357	44,326***
distress	Pain cluster	,096	,278	2,653	,010	,188	,178	17,382***
	Fatigue cluster	.083	.548	5.756	.000	.301	.292	33.130***

*** p<.001

Figure 3

Figure4. Factors affecting the participants' symptom intensity cluster (N=79)

Factor	Cluster	B	b	t	p	R^2	Adj R^2	F
Psycho-social	Fatigue cluster	,089	,558	8,103	,000	,338	,329	39,918***
distress	Emotional disturbance cluster	,067	,546	5,876	,000	,359	,350	42,525***
	Cognitive impairment cluster	.065	.484	4.858	.000	.234	.224	23.661***
	Pain cluster	,064	,480	4,594	,000	,230	,218	19,991***

*** p<.001

Figure 4

PO08-20

VALIDITY AND RELIABILITY OF KOREAN VERSION OF THE ONCOLOGY PATIENTS PERCEPTION OF THE QUALITY OF NURSING CARE SCALE (OPPQNCS) FOR WOMEN WITH BREAST CANCER

Jiyoung Kang[1*], **Eunyoung Eunice Suh**[2*], **Youngmee Kim**[1], **Hyeyoung Kang**[1], **Nanyeon Kim**[1], **Mijung Lee**[1], **Eugene Kim**[1], **Juhyeon Kim**[1], **Sujeong Yeo**[1], **Yunye Seo**[1]

[1] *Dept. of Nursing, Seoul National Univ. Hospital, Korea*
[2] *College of Nursing, Seoul National Univ., Korea*

Background/Purpose : Breast cancer is the most common malignant neoplasm among women in South Korea. The purpose of this methodological study was to examine the reliability and validity of a translated Korean version of The Oncology Patients Perception of the Quality of Nursing Care Scale (OPPQNCS). The OPPQNCS was developed from a qualitative study-generated middle range theory to measure the quality of cancer nursing care from the patients' perspective. The OPPQNCS comprises four subscales: responsiveness, individualization, coordination, and proficiency.

Methods : A cross-sectional survey design was used. A total of 200 women with breast cancer were recruited in an urban cancer center in South Korea. Self-reported questionnaires were administered to each participant while they were hospitalized in oncology ward for the purpose of mass removal surgery. The Korean OPPQNCS was articulated through forward-backward translation methods. The permission for the use of the OPPQNCS was obtained from the original developer. The data were currently under analysis using SPSS (version 20.0) and AMOS (version 20.0). Internal consistency reliability, construct and criterion validity will be calculated.

Results : The results of the study will report the Korean version of OPPQNCS show reliable internal consistency. Factor loadings of the 41 items on the four sub-scales for the Korean OPPQNCS will be validated among breast cancer women by the time of this presentation.

Conclusion : Results of this study will demonstrate that the reliability and validity of a translated Korean version of The OPPQNCS can be used as a reliable and valid scale to measure cancer nursing care quality from the patient's perspective surrounding breast cancer patients at the time of immediate post-operational period. By revealing patient's perception of the quality of nursing care, a more comprehensive and tailored nursing intervention can be developed.

PO08-21

CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY: KOREAN ONCOLOGY NURSES' KINOWLEDGE AND PRACTICE

Jeong Hee Kang, Hye Young Kim, Sung Reul Kim

College of Nursing, Chonbuk National Univ., Korea

Background/Purpose : This study explored the level of knowledge and practice behaviors regarding chemotherapy-induced peripheral neuropathy (CIPN) in a group of oncology nurses in Korea.

Methods : A convenience sample of 62 Korean oncology nurses participated in this cross-sectional descriptive survey. Nurses were invited to participate in the study if they were currently taking of cancer patients at hospital-based outpatient infusion centers or inpatient units where chemotherapy agents were administered to cancer patients. Data were collected with self-report questionnaires about knowledge and practice behaviors regarding CIPN.

Results : The levels of knowledge and practice behaviors for recognizing and assessing patients at high risk for or experiencing CIPN symptoms, and to plan and implement nursing cares to prevent, minimize, or preferably reverse CIPN symptoms were not satisfactory.

Conclusion : Study results showed the need to improve currently practicing oncology nurses' knowledge and practices in routinely assessing and managing CIPN symptoms.

PO08-22

FACTORS AFFECTING SYMPTOM EXPERIENCES OF BREAST CANCER PATIENTS: BASED ON THE THEORY OF UNPLEASANT SYMPTOMS

Hyojin Kim[1*], **Sanghee Kim**[2], **Hyangkyu Lee**[2], **Sangeun Oh**[3]

[1] *Dept. of Oncology Nursing, Graduate School of Nursing, Yonsei Univ., Korea*
[2] *College of Nursing, Yonsei Univ., Korea*
[3] *College of Nursing, Chonnam National Univ., Korea*

Background/Purpose : For the quality of life, it needs for cancer patients to be controlled their symptoms and factors affecting symptoms. The purpose of this study was to identify the factors affecting symptom experiences of breast cancer patients.

Methods : A cross-sectional descriptive study was conducted. Sixty breast cancer patients were recruited. We measured their symptom experiences, physiologic factors (immune system function and specific perceived symptoms regarding breast cancer), psychological factors (depression and anxiety) and situational factors (family support). After obtaining permission from the IRB, data were collected from self-report questionnaires and electronic medical records from a single cancer center. Descriptive statistics, t-test, one-way ANOVA, correlations and multiple regressions were used to analyze the data.

Results : The mean score for the symptom experiences were relatively moderate (mean±SD, 58.35±42.17). The most frequent and severe symptoms were fatigue (4.47±2.99), numbness or tingling (3.67±3.08) and sadness (3.45±3.64). Symptom experiences were significantly positively correlated with psychological factors ($r=0.671$, $p<0.01$) and physical symptoms ($r=0.392$, $p<0.01$). Symptom experiences and situational factors ($r=0.297$, $p<0.05$) were had a significantly negative correlation. The factor that had the most impact on symptom experiences were psychological factors, followed by perceived physical symptoms. The regression model explained 53.2% of the variances.

Conclusion : In conclusion, the results showed that symptom experiences were affected by physiological and psychosocial factors. This was in-line with the theory of unpleasant symptoms. Based on the results of this study, the physiological, psychological and situational factors should be considered for tailored nursing interventions.

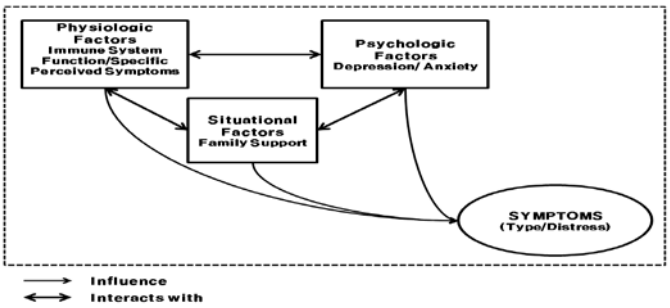

Figure 1

PO08-23

STUDY ON CANCER PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT DUE TO CHEMOTHERAPY INDUCED SIDE EFFECTS

Soojung Lim[1], **Myungsun Yi**[2*]

[1] *Dept. of Nursing, Seoul St. Mary's Hospital, Korea*
[2] *College of Nursing, Seoul National Univ., Korea*

Background/Purpose : The number of cancer patients visiting emergency department has increased recent years mainly due to the increase of outpatient-based chemotherapy and the shortness of hospital stay. The purpose of this study was to identify conditions of cancer patients who visited emergency department due to the side effects of chemotherapy.

Methods : Retrospective descriptive study design was used. Data were collected from medical records of 294 cancer patients who visited a tertiary university hospital in Seoul, resulting from the side effects of chemotherapy in 2009. The data were collected in terms of emergency department visit-related characteristics and the side effects of chemotherapy. The data were analyzed using descriptive statistics, t-test, one way ANOVA, and Scheffe's test.

Results : The incidence of emergency department visits due to the side effects of chemotherapy as a chief complaint was 15.2% of all cancer patients who visited emergency department. The most common type of cancer was lung cancer (16.7%), and that of chemotherapy was alkylating agents (53.1%). The elapsed days to emergency department visit after receiving chemotherapy were 9.6 in average. Grade 3 was the most common group (81.6%) in terms of emergency department Triage Acuity Scale. The ratio of the hospitalization after emergency treatment was 72.8% and the average stay of the hospitalization was 9.2 days. In the end, 93.5% were discharged from the hospital but 6.5% were dead. The most frequent type of side-effect of chemotherapy was decreased platelet count (80.6%), followed by anemia (74.5%), pain (52.0%), decreased neutrophil count (50.7%), and decreased white blood cell count (46.3%). Hospitalization group after emergency treatment was higher than the discharge group ($p=0.020$) in terms of the decreased white blood cell count. The group of death had higher scores of cough and dyspnea compared to the discharge group after hospitalization ($p<0.05$).

Conclusion : In conclusion, most subjects (approximately 3/4) who visited emergency department due to side effects of chemotherapy were admitted to the hospital after emergency treatments. And about 6.5% were dead in the end. It suggests that there is a special need to create a system to manage symptoms effectively. Also it is necessary to provide a prompt initial evaluation and appropriate care and treatment for cancer patients when they present to emergency department with side effects of chemotherapy. In addition, more effective discharge education program should be provided to cancer patients with chemotherapy to help them cope with side effects at home.

PO08-24

EFFECT OF ZOLADEX® ON PSYCHOPHYSICAL SYMPTOMS IN PREMENOPAUSAL BREAST CANCER WOMEN TREATED WITH TAMOXIFEN WITHOUT ADJUVANT CHEMOTHERAPY: A PILOT STUDY

Jiyoung Kim[1], **Juhee Cho**[2], **Eun-Kyung Choi**[2], **Won Ho Kil**[1], **Seok Won Kim**[1], **Jeong Eon Lee**[1], **Seok Jin Nam**[1]

[1] *Division of Breast and Endocrine Surgery, Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

[2] *Cancer Education Center, Samsung Comprehensive Cancer Center, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

Background/Purpose : Gonadotropin-releasing hormone agonists (Zoladex®) have been shown to be one of the therapeutic options as an effective adjuvant therapy for hormone receptor-positive early breast cancer patients. However, psychophysical adverse effect of Zoladex® has not been fully appreciated. The aim of this study was to assess the effects of Zoladex® on the menopausal symptoms and perception of anxiety and depressive symptoms.

Methods : Between July 2010 and July 2011, we prospectively recruited patients who had undergone surgery for hormone-responsive stage I breast cancer, who were premenopausal aged 50 years or under, and who were expected to receive adjuvant tamoxifen therapy without chemotherapy (n=39). Study participants were classified as Group A (tamoxifen only use, n=23) and Group B (tamoxifen with Zoladex® use, n=16). With help from a trained interviewer, study participants completed questionnaires on psychological and physical menopausal symptoms (Menopause Rating Scale, MRS), and anxiety and depression (the Hospital Anxiety and Depression Scale, HADS) sequentially at enrollment (adjuvant treatment begin), 3 months, 6 months, 12 months, and 24 months after treatment. Socio-demographic and clinical characteristics were also assessed. To examine changes overtime, mixed effect analysis was performed using STATA 12.

Results : Baseline socio-demographic characteristics between two groups were not different except for participants' age (45.1±3.3 vs. 42.4±4.1, $p<0.05$). When assessing the pattern of psychological and physical menopausal symptoms with MRS score, both two groups reported higher symptom score of each domain from the baseline over time during the treatment period (p-value for trend <0.05, respectively). At 6 months after treatment, patients that were administered tamoxifen with Zoladex® reported significantly higher overall mean score than those treated with only tamoxifen (7.4±1.7 vs. 13.9±1.7, $p=0.02$). Especially, somatic symptom scores showed significant difference between two groups at 3 and 6 months (2.3±0.7 vs. 4.6±0.9, $p=0.02$ at 3 months, 2.8±0.7 vs. 5.2±0.9, $p=0.02$ at 6 months). At 0 to 24 months, Zoladex® itself did not have a significant effect on patients' perceived anxiety and depressive symptoms by HADS, and caused more severe depression symptom only at 12 months (7.9±0.9 vs. 10.3±1.2, $p=0.02$).

Conclusion : Zoladex® aggravated menopausal symptoms during adjuvant endocrine therapy of premenopausal breast cancer patients, especially somatic symptoms. Most obvious adverse effect of Zoladex® appeared at 6 months after treatment. Therefore proper physical intervention should be considered before that time for psychophysical well-being of patients treated with Zoladex®.

PO08-25

TECHNOLOGY VERIFIED CHANGES OF SKIN DRYNESS AND PIGMENTATION DURING CHEMOTHERAPY

Dan Bee Kang[1], **Im-Ryung Kim**[2], **Eun-Kyung Choi**[2], **Soo Jung Park**[1], **Seok-Jin Nam**[3], **Jeong Eon Lee**[3], **Won Ho Gil**[3], **Se-Kyung Lee**[3], **Juhee Cho**[4*]

[1] *Dept. of Health Sciences and Technology, Sungkyunkwan Univ., Samsung Advanced Institute for Health Sciences and Technology, Korea*

[2] *School of Medicine, Sungkyunkwan Univ., Cancer Education Center, Samsung Comprehensive Cancer Center, Samsung Medical Center, Korea*

[3] *Dept. of Surgery, School of Medicine, Sungkyunkwan Univ., Samsung Medical Center, Korea*

[4] *Dept. of Health Sciences and Technology, School of Medicine, Sungkyunkwan Univ., Samsung Advanced Institute for Health Sciences and Technology, Korea*

Background/Purpose : While chemotherapy-induced altered appearance is one of the most painful side effects of chemotherapy, skin dryness and darkness are still major side effects with no successful preventive interventions. Yet there is not much known about the definite mechanism of skin changes due to chemotherapy, and previous studies were limited to assess patient reported outcomes. This study aimed to evaluate skin dryness and pigmentation throughout chemotherapy using validated cosmetic devices.

Methods : This study was a prospective cohort study which assessed skin conditions of 81 patients in 4 groups by stage (stage 0, I, II, and III). The assessments were conducted before, during, 1 month, 2~3 months and 6 month after chemotherapy. We measured moisture contents, sebum, Trans epidermal Water Loss (TEWL), and melanin on face and hands using Corneometer, Subumeter, Vapometer, and Mexameter. We also assessed patient reported dryness, darkness and health-related quality of life due to skin problems using Dermatology Life Quality Index (DLQI).

Results : Of total 16 (26.2%) received four cycles of adjuvant doxorubicin/cyclophosphamide (AC), 16 (26.3%) and 29(47.5%) received doxorubicin, cyclophosphamide, 5-fluorouracil (FAC) and four cycles of AC plus four cycles of paclitaxel (AC+T) respectively. Another 20 patients only received adjuvant endocrine therapy. With patients with chemotherapy, sebum and TEWL were significantly decreased after chemotherapy and the melanin level significantly increased from baseline. Those poor skin conditions were not fully recovered and water level got worse 6 month after chemotherapy. Both patients with chemotherapy and endocrine therapy experienced skin changes and patients with chemotherapy had significantly worse skin dryness (lower sebum) and pigmentation (higher melanin) compared to patients only with endocrine therapy. Objective changes detected by cosmetic devices were linear with patients reported outcomes, and more skin changes patients experienced, worse quality of life due to skin problems they had. All of these were statistically significantly after adjusting demographic and clinical characteristics.

PO08-25

Conclusion : This is the first study that assessing chemotherapy-induced skin dryness and pigmentation using high validated high-tech cosmetic devices. This study confirms that patients experienced dramatic skin changes due to chemotherapy resulting in poor dermatology quality of life. Further study is necessary to find exact mechanism of melanin and sebum changes due to chemotherapy and develop more active interventions for preventing or managing cancer treatment induced skin problems.

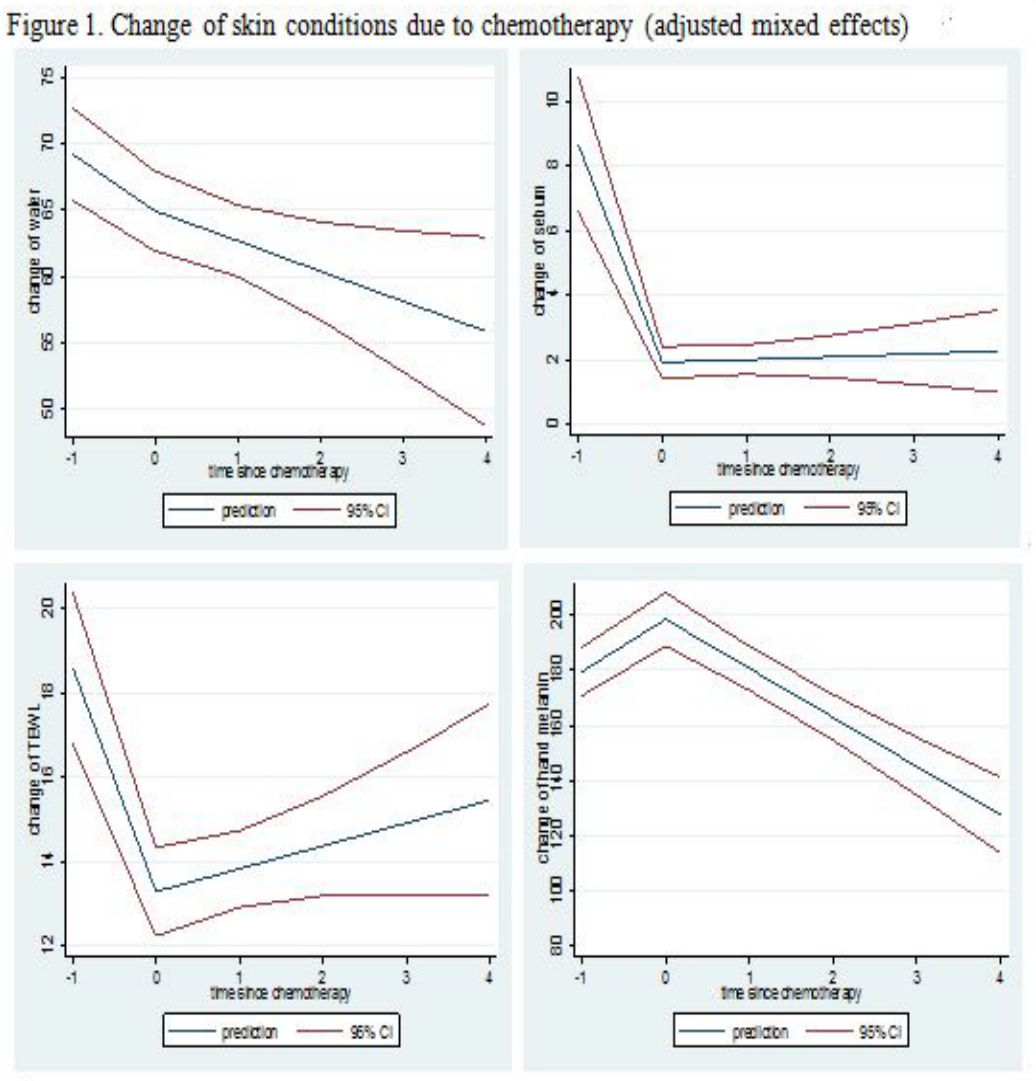

Figure 1

PO08-25

Table 1. Change of skin change due to chemo therapy

	Baseline	Chemo #2	Chemo #7	Post chemo 1m	Post chemo 3m
	Coef [95% CI] (vs. baseline adjusted age and baseline score)				
	Water Mean (SD)				
Hormone	61.8 (11.6)	67.1 (6.5)		71.9 (15.5)	57.8 (17.4)
Coef; 95% CI	Reference	5.3; -2.2 to 12.9	-	10.0; 2.4 to 17.7	-4.7;-12.9 to 3.5
p-value	-	0.17		0.01	0.3
Chemo	69.2 (12.4)	64.1 (15.1)	62.8 (12.4)	63.5 (13.3)	61.4 (19.5)
Coef 95% CI	Reference	-4.6; -9.8 to 0.6	-6.4; -13.4 to 0.6	-5.7; -10.9 to -0.4	-7.9; -13.3 to -2.5
p-value	-	0.08	0.07	0.04	0.004
Between Group Difference in Mean change (vs. Hormone)‡	7.7 (*p*<0.001)	-9.1 (*p*<0.001)		-15.5 (*p*<0.001)	-0.6 (*p*=0.8)
	Sebum Mean (SD)				
Hormone	6.4 (10.3)	3.5 (4.5)		3.2 (3.1)	2.1 (2.5)
Coef; 95% CI	Reference	-2.9; -5.7 to 0.0	-	-3.4; -6.4 to -0.4	-4.8;-8.0 to -1.7
p-value‡	-	0.05		0.03	0.003
Chemo	8.1 (8.9)	2.3 (2.9)	1.7 (2.5)	2.1 (2.7)	2.1 (3.2)
Coef 95% CI	Reference	-6.6; -8.2 to -5.0	-3.3; -9.9 to 3.3	-7.2; -8.8 to -5.6	-6.8; -8.5 to -5.2
p-value‡	-	<0.001	0.33	<0.001	<0.001
Between Group Difference in Mean change (vs. Hormone)§	2.4 (*p*<0.001)	-3.7 (*p*<0.001)		-3.7 (*p*<0.001)	-2.0 (*p*=0.06)
	TEWL Mean (SD)				
Hormone	16.4 (6.2)	13.3 (5.7)		16.2 (6.6)	15.2 (6.9)
Coef; 95% CI	Reference	-3.1; -5.4 to -0.8	-	-0.6; -2.9 to 1.8	-0.7;-3.3 to 1.9
p-value‡	-	0.008		0.65	0.60
Chemo	18.6 (7.0)	13.7 (4.7)	12.5 (3.6)	12.5 (3.6)	14.6 (6.5)
Coef 95% CI	Reference	-4.1; -5.8 to -2.4	-6.4; -8.5 to -4.3	-6.0; -7.7 to -4.3	-4.1; -5.9 to -2.4
p-value‡	-	<0.001	<0.001	<0.001	<0.001
Between Group Difference in Mean change (vs. Hormone)§	2.2 (*p*=0.003)	-0.7 (*p*=0.27)		-5.0 (*p*<0.001)	-4.4 (*p*<0.001)
	Melanin (Hand) Mean (SD)				
Hormone	199.7 (39.1)	208.4 (39.1)		198.3 (45.5)	177.8 (46.3)
Coef ; 95% CI	Reference	8.7; -3.7 to 21.1	-	-0.3; -12.9 to 12.3	-22.0;-35.7 to -8.4
p-value‡	-	0.17		0.97	0.002
Chemo	179.6 (35.7)	197.9 (43.1)	98.8 (58.6)	184.5 (39.3)	158.6 (32.0)
Coef 95% CI	Reference	23.0; 13.6 to 32.3	27.2; 7.6 to 46.8	5.0; -4.4 to 14.5	-20.6; -30.3 to -11.0
p-value‡	-	<0.001	0.007	0.29	<0.001
Between Group Difference in Mean change (vs. Hormone)§	-20.2 (*p*<0.001)	13.8 (*p*<0.001)		4.1 (*p*=0.29)	1.6 (*p*=0.70)

†Hormone group at baseline (n=20), chemo (n=20), post chemo 1month (n=19) and post chemo 3 month (n=15), and Chemo group at baseline (n=61), chemo #2 (n=57), chemo #7 (n=29), post chemo 1 month (n=57), and post chemo 3 month (n=53)

‡ Chemo, post chemo 1month and 3month compared to baseline

Table 1

PO08-26

CHANGE OF QUALITY OF LIFE AND SYMPTOM EXPERIENCE IN BREAST CANCER PATIENTS WITH CHEMOTHERAPY

Jin-Hee Park, Sun Hyoung Bae*, Youngmi Jung

College of Nursing, Ajou Univ., Korea

Background/Purpose : Women diagnosed with breast cancer face significant side-effects due to aggressive adjuvant chemotherapy regimens. These side effects adversely impact patient quality of life and symptom experience. The purpose of the study was to describe the change in quality of life and symptom experience among breast cancer patients with chemotherapy.

Methods : Sixty six breast cancer patients who had surgery and planned adjuvant chemotherapy recruited from a medical center. Patients were assessed with quality of life (the functional assessment of cancer therapy for breast cancer, FACT-B) and symptom experience (Memorial Symptom Assessment Scale-Short Form, MSAS-SF) before chemotherapy (pretest), after chemotherapy (posttest), and 6 months after chemotherapy (follow-up test). Analysis of variance of repeated measures was used to investigate the change of quality of life and symptom experience.

Results : On average, the breast cancer patients were approximately 46 years of age, and experienced partial mastectomy, radiotherapy, and hormone therapy. According to results of repeated measure ANOVA, FACT-B total score declined at post-test but were near baseline at follow-up test ($F=8.15$, $p=0.001$). Among the subscales of FACT-B total, physical well-being ($F=6.75$, $p=0.003$) and breast cancer subscale ($F=21.06$, $p<0.001$) showed similar trends. On the other hand, the score of social well-being significantly decreased over time from pretest to 6 months after chemotherapy ($F=5.96$, $p=0.003$). However, there was no statistically significant interval change in the emotional well-being subscale. In symptom experience, TMSAS (Scoring Maternal Separation Anxiety Scale) score increased at posttest but decreased at follow-up test ($F=19.93$, $p<0.001$). Both physical and psychological symptom subscales also showed similar trends ($F=11.11$, $p<0.001$; $F=3.91$, $p=0.027$, respectively). Score of psychological symptom subscales at the follow-up test was higher than at pretest (mean difference -0.12, 95% CI -0.11 to 0.34), however, the score of physical symptom subscale was similar with at pretest (mean difference -0.03, 95% CI -0.20 to 0.14).

Conclusion : Breast cancer patients were suffered side effects from chemotherapy, and experienced worse quality of life. Though physical symptom and well-being recovered, patients had poorer social and emotional well-being until 6 months after chemotherapy. When considering the substantial increase in life expectancy in persons with breast cancer, nursing practice and research have to focus on their quality of life and give positive psychological intervention to improve the symptom experience and quality of life.

PO08-27

PACLITAXEL CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY AND QUALITY OF LIFE IN POSTOPERATIVE BREAST CANCER PATIENTS

Hye Young Kim[1*], **Jeong Hee Kang**[1], **Hyun Jo Youn**[2], **Chi Eun Song**[3]

[1] *School of Nursing, Chonbuk National Univ., Korea*
[2] *Dept. of Surgery, Chonbuk National Univ. Medical School, Korea*
[3] *Dept. of Hematology, Chonnam National Univ. Hwasun Hospital, Korea*

Background/Purpose : Paclitaxel is among the most useful anticancer agents used in postoperative adjuvant chemotherapy for node-positive breast cancer. But one of the common and serious side effects is peripheral neuropathy. Peripheral neuropathy is a dysfunction of motor, sensory, and/or autonomic neurons and results in peripheral neuropathic signs and may have a negative impact on quality of life. This study was performed to identify how patients experienced paclitaxel chemotherapy-induced peripheral neuropathy (PCIPN) and quality of life related to PCIPN.

Methods : A total of 82 women with chemotherapy-induced peripheral neuropathy participated in this study. Data were collected through self-reported questionnaire which were constructed to include European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, QLQ-BR23, and QLQ-CIPN20. Data were analyzed using SPSS/WIN20 for descriptive statistics, t-test, ANOVA, Duncan, and Pearson's correlation coefficients.

Results : The mean score for each subcategory of QLQ-C30 was 46.14 for global health status, 62.43 for functional scales, and 31.29 for symptom scales. The mean score for each subcategory of QLQ-BR23 was 56.55 for functional scales and 42.06 for symptom scales. And also, the mean score of sensory scales was 30.42, motor scales was 24.03, and autonomic scales was 22.70 in the CIPN20. In CIPN20, the sensory scale showed significant differences according to Eastern Cooperative Oncology Group Performance status (ECOG PS), duration of diagnosis, current chemotherapy status, and duration of CIPN. The motor scale showed significant differences according to occupation and ECOG PS. And the autonomic scale showed significant differences according to occupation, education, ECOG PS, and current chemotherapy status. There was a significant correlation with QOL and peripheral neuropathy scales (r=-0.42 to r=-0.62).

Conclusion : The quality of life subscales had a moderate correlation with the PCIPN subcategories in postoperative breast cancer patients. There is a need for developing an intervention for breast cancer patients to enhance their quality of life and to alleviate chemotherapy-induced peripheral neuropathy.

PO08-28

RELIABILITY AND VALIDITY OF THE KOREAN VERSION OF THE EORTC QUALITY OF LIFE QUESTIONNAIRE TO ASSESS CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY : THE QLQ-CIPN20

Hye Young Kim[1*], **Jeong Hee Kang**[1], **Hyun Jo Youn**[2], **Sung Hoo Jung**[2], **Hyang Sook So**[3], **Sung Reul Kim**[1]

[1] *School of Nursing, Chonbuk National Univ., Korea*
[2] *Dept. of Surgery, Medical School, Chonbuk National Univ., Korea*
[3] *School of Nursing, Chonnam National Univ., Korea*

Background/Purpose : Chemotherapy-induced peripheral neuropathy (CIPN) is a major, potentially dose-limiting side effect of several chemotherapeutic agents and may seriously affect patients' quality of life. But, CIPN is both under-assessed and under-reported and few self-report tools exist that assess CIPN. Self-report tool, the QLQ-CIPN20 sub-scale composed of 20 items designed to evaluate the severity and impact of neuropathy symptoms on cancer patients' lives. This study was performed to develop a Korean version of the EORTC QLQ-CIPN20 for measuring chemotherapy induced peripheral neuropathy and to verify both reliability and validity of the Korean version.

Methods : The EORTC QLQ-CIPN20, EORTC QLQ-C30 version 3.0, and Eastern Coopered Oncology Group (ECOG) performance status tools were administered to 249 cancer patients with CIPN-related symptoms recruited from two university hospitals. Collected data were analyzed using SPSS 20.0 and AMOS 20.0. Construct validity (confirmatory factor analysis), items convergent and discriminant validity, known-groups validity, concurrent validity, and internal consistency reliability of the QLQ-CIPN20 Korean version were evaluated.

Results : Factor analysis confirmed the three dimensions of CIPN: sensory, motor and autonomic. Factor loading of the 20 items on the three sub-scales ranged from 0.38 to 0.83. The three subscales model was validated by confirmatory factor analysis (GFI=0.90, AGFI=0.86, RMSEA=0.05, NFI=0.87, and CFI=0.94). The QLQ-CIPN20 also established items convergent and discriminant validity, and known-group validity. Furthermore, QLQ-CIPN20 demonstrated a concurrent validity with EORTC QLQ-C30. The Cronbach's alpha coefficient for internal consistency of the sub-scales ranged from 0.73 to 0.89.

Conclusion : The Korean version of EORTC QLQ-CIPN20 showed satisfactory construct, concurrent, known-group validity, and internal reliability.

PO08-29

COGNITIVE FUNCTION IN BREAST CANCER SURVIVORS RECEIVING CHEMOTHERAPY

Jung-Hoon Jung[1], Mi-Young Kang[1], Hyun-Ju Kim[1], Eun-Young Jun[2*]

[1] *Dept. of Nursing, Cheil General Hospital & Women's Healthcare Center, Korea*
[2] *Dept. of Nursing, Daejeon Univ., Korea*

Background/Purpose : Many problems of breast cancer survivors are occurred to cancer treatment that may experience cognitive changes particularly those treated with chemotherapy. These problems commonly affect executive functions and significantly reduce quality of life. The purpose of this study was to examine the level of the cognitive function, and to identify the influence factors on cognitive function in breast cancer survivors receiving chemotherapy. This study attempted to provide basic data useful to development of nursing intervention and improve the quality of life in breast cancer survivors.

Methods : As a cross-sectional descriptive study, women with receiving chemotherapy above one cycle were recruited to participate. Following IRB approval, participants were recruited from inpatients of one hospital in Seoul, Korea. Self-report questionnaires were administered to measure cognitive function, quality of life, depression, and anxiety.

Results : This study is ongoing and preliminary finding will be reported. Analysis measures are as follows: Descriptive statistics and correlation coefficients will be examined. Comparisons among cognitive function according to related factors will be performed by t-test and ANOVA. And influence factors of cognitive function will be confirmed by multiple regressions.

Conclusion : The findings of this study are expected to provide basic information on cognitive function among breast cancer survivors receiving chemotherapy, and inform future related to cognitive intervention and supportive measures to prevent and manage impaired cognitive function.

PO08-30

THE CLINICAL IMPERATIVES OF CANCER-RELATED FATIGUE SYMPTOM CLUSTERS AMONG KOREAN WOMEN WITH BREAST CANCER

Sue Kim[1], **Keon Suk Lee**[2], **Kyung Hee Lee**[3], **Eun Kyung Hwang**[4], **Hye Jin Joh**[5], **Kyung Hee Lim**[6], **Dong Mi Kim**[2], **Yun Hee Ko**[1], **Jee Hee Han**[1]

[1] *College of Nursing, Yonsei Univ., Korea*
[2] *Breast Cancer Center, National Cancer Center, Korea*
[3] *Breast Cancer Clinic, Severance Hospital, Korea*
[4] *Breast Care Center, Seoul National Univ. Hospital, Korea*
[5] *Dept. of General Surgery, Seoul St. Mary's Hospital, Korea*
[6] *College of Nursing, Keimyung Univ., Korea*

Background/Purpose : Cancer-related fatigue (CRF) is the most common symptom experienced by 50-90% cancer patients across the cancer trajectory, and is reported to have a major impact on quality of life. Prior breast cancer CRF studies have lacked inclusion of patients after completion of active treatment, and how factors such as age, anti-hormonal therapy, and cognitive decline may be interrelated with long-term CRF. Although the literature suggests a psychoneurologic symptom cluster for CRF in Caucasian breast cancer patients, there have been no studies exploring how CRF symptom clusters present in Korean women following a diagnosis of breast cancer. As the prevalence and contextual factors of breast cancer in Korea differ from the West, this study aimed to identify symptom clusters related to CRF in Korean breast cancer survivors.

Methods : This study is a cross-sectional descriptive study of women with breast cancer recruited from five major hospitals across Korea. Inclusion criteria included aged 20-69 years, stages I-III, currently undergoing or having finished chemotherapy and/or radiation therapy; and within 6 years of diagnosis. Women with underlying diseases, psychiatric problems, and recurrent cancers were excluded. After IRB approval, self-report questionnaires were administered to measure CRF, depressive mood, sleep quality, cognitive dysfunction, pain, menopausal symptoms, and social support.

Results : This study is ongoing with data expected to be obtained from 400 participants by August, 2013. Preliminary analysis of current data (n=181) suggest a moderate level of CRF among participants, with notable differences in severity by sub-dimensions. Although 64.6% of respondents were found to have depressive mood state, subjective QOL and health status was rated as moderately fair. CRF was significantly correlated with psychological factors, physical factors, perceptual factors, and cognitive function, particularly with depressive mood, physical menopausal symptoms, and emotional menopausal symptoms. Upon completion of data collection, symptom clusters will be determined by which symptoms significantly loaded by common factor analysis and squared multiple correlation will be computed to measure communality. Comparisons among symptom clusters according to hormone therapy use will be performed by ANOVA.

PO08-30

Conclusion：The findings of the study are expected to enrich our understanding of CRF among Korean breast cancer survivors, especially in relation to hormone therapy use and across the cancer trajectory. Findings can inform nurses and other health care professionals in targeting key areas and time points for educational interventions and supportive measures to prevent and manage CRF.

PO08-31

THE EFFECT OF SPIRITUAL INTERVENTIONS ON DEPRESSION, ANXIETY, SPIRITUAL WELL-BEING AND PAIN OF ONCOLOGY PATIENTS: A META-ANALYSIS

Pok-Ja Oh, Suk-Jung Han

Dept. of Nursing, Sahmyook Univ., Korea

Background/Purpose : The purpose of this study was to evaluate the effectiveness of spiritual interventions on depression, anxiety, spiritual well-being and pain in cancer patients.

Methods : A total of 1070 studies were retrieved from electronic databases. From these studies, fourteen studies met the inclusion criteria with a total of 734 participants. Methodological quality assessed by The Cochrane's Risk of Bias (RoB) and Methodological Items for Non randomized Studies (MINORS). The data were analyzed by the RevMan 5.2 program of Cochrane library.

Results : Overall effect size of spiritual interventions on depression was high (-1.75) and publication bias was detected as evaluated by funnel plot. The effects on anxiety, spiritual well-being, and pain were -0.88, -1.12, -0.78, respectively. Studies with terminal cancer patients had larger effects compared to studies that applied to non-terminal cancer patients.

Conclusion : This study suggests that spiritual interventions can relieve depression, anxiety and spiritual well-being in terminal cancer patients. However, more well-designed studies are needed.

PO08-32

DEVELOPMENT AND EVALUATION OF A SEXUAL HEALTH IMPROVEMENT PROGRAM FOR WOMEN WITH GYNECOLOGIC CANCER

Soon Yang Jang[1], **Jeong Sook Park**[2*]

[1] *Dept. of Nursing Graduate, Keimyung Univ., Korea*
[2] *College of Nursing, Keimyung Univ., Korea*

Background/Purpose : The purpose of this study was to develop a sexual health improvement program for women with gynecologic cancer and also to evaluate the effects of the program.

Methods : The improvement program was developed based on a needs assessment derived from an in-depth interview, analysis of the literature, and the predictive factors of sexual function in women with gynecologic cancer which I conducted as previous study. The sexual health improvement program was comprehensively constructed reflecting the conceptual framework of sexual health by Cleary, Hegarty, & McCarthy (2011), including sexual function, sexual self-concept and sexual relationship. This program consisted of information about sexuality, Kegel exercises, group art activities, psychodrama and group counseling. Evaluation of the program was conducted under the principle of quasi-experimental design. Women with gynecological cancer who had completed their cancer treatment were recruited by telephone at A University Hospital in D city in Korea. Subjects (n=30) were assigned to two groups: the experimental group (n=15) participated in the sexual health improvement program for 2 hours, once a week for 6 weeks, and the control group (n=15) received a general educational program for gynecological cancer at 1, 3, and 6 weeks. Sexual function was measured by the Female Sexual Function Index (FSFI), sexual self-concept was measured by the Body Image Questionnaire and the Draw A Person (DAP) test, and sexual relationship was assessed by the Sexual Communication Questionnaire. Data were analyzed using SPSS/WIN 18.0. In addition, the outcome of the DAP test was analyzed by an expert in art psychotherapy.

Results : Both post-test scores of total FSFI ($p<0.001$) and all subscale scores including sexual desire ($p<0.001$), arousal ($p=0.001$), lubrication ($p=0.004$), orgasm ($p=0.001$), satisfaction ($p=0.001$), and pain ($p=0.009$) in the experimental group showed significantly greater improvement than in the control group. The experimental group showed significantly higher post-test scores in body image than those of the control group ($p=0.009$) and showed an improvement in body image on the DAP test after the sexual health improvement program. Also, the experimental group showed significantly higher post-test scores in sexual communication than those of the control group ($p<0.001$).

Conclusion : A sexual health improvement program can contribute to improving the sexual health and quality of life of women with gynecologic cancer. In addition, the results of this study can be used as baseline data for the development of future sexual health intervention methods relevant to Korean culture. Finally, strategic development that can facilitate the dissemination of information about sexual health improvement programs for women with gynecologic cancer is highly recommended.

PO08-33

FACTORS RELEVANT TO UPPER EXTREMITY FUNCTIONS AND HEALTH RELATED QUALITY OF LIFE IN WOMEN AFTER BREAST CANCER SURGERY

Chie Furukawa[1*], **Takashi Morimoto**[2], **Takashi Nomura**[2], **Ikuharu Morioka**[3]

[1] *Faculty of Nursing, Taisei Gakuin Univ., Japan*
[2] *Dept. of Breast Surgery, Yao Municipal Hospital, Japan*
[3] *Graduate School of Health and Nursing Science, Wakayama Medical Univ., Japan*

Background/Purpose : The purpose of this study is to clarify factors relevant to upper extremity functions and Health Related Quality of Life (HRQOL) in patients after breast cancer surgery.

Methods : The participants were 87 patients after breast cancer surgery who signed informed consent forms at a municipal hospital in Osaka, Japan. Data were gathered by semi-structured interviewing. The upper extremity functions were evaluated by DASH (JSSH; 30 questions). HRQOL was evaluated by QOL-ACD-B (21 questions). The interview was conducted before the previous day of surgery, discharge day, 4 week, 12 week, 150 day after surgery (±7 day), and 1 year after surgery (±14 day). The questionnaire included age, operation method, status of axillary lymph node dissection, radiotherapy, chemotherapy and support person status, etc. We used multiple linear regression analysis to find the factors relevant to the change in DASH and QOL-ACD-B scores.

Results : All participants were women. The average age was 60.4 years. DASH and QOL-ACD-B scores changed over time as shown figure 1. The DASH score was the lowest at the discharge day, but it increased after that. On the other hand, QOL-ACD-B score shows the lowest at the 12 week and increased gradually after that. The axillary lymph node dissection was the declining factor of DASH score at the 4 week. The chemotherapy was its declining factor at the 12 week and the 150 day. The radiotherapy was the factor decreasing QOL-ACD-B score at 1 year.

Conclusion : This study clarified the factors that nurses give importance to in their activities to help the patients at the various time after breast cancer surgery.

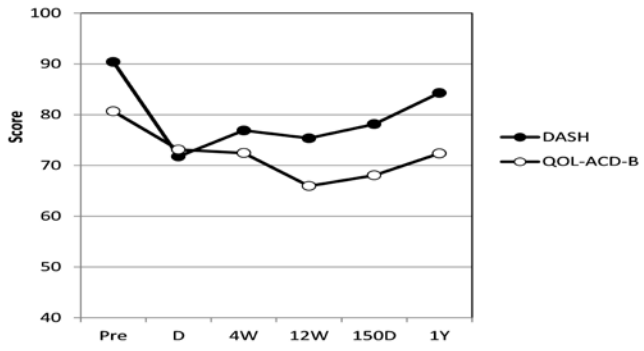

Figure 1

PO08-34

SHARED MEDICAL DECISION-MAKING ABOUT CANCER PATIENT'S CRITICAL SELECTION

Hyang Sook So[1], **Ae Ran Park**[2], **Myeong Jeong Chae**[3]

[1] *College of Nursing, Chonnam National Univ., Korea*
[2] *Dept. of Nursing in Graduate School, Chonnam National Univ., Korea*
[3] *Dept. of Nursing, Gwangju Woman's Univ., Korea*

Background/Purpose : The purpose of this study is to identify the difference between the score of shared medical decision-making of physicians and the one of nurses, and also, to identify the responses of medical staffs about two questions 'Who should be notified first cancer diagnosis? Who should be made final decision in critical situations?' After the year of 2010, a single person household is rapidly growing and the first order of size of a family in Korea. Person, esp. young people who lives alone places his or her own on priority to make decisions because self-own is an independent person with fundamental human rights.

Methods : A total of one hundred people who are physicians and nurses were recruited from a regional national cancer center. The shared medical decision-making scale was self-reported questionnaire, which be composed of 34 items and 5 points likert scale (Jo, K.H., 2012). The collected data were analyzed by t-test, one-way ANOVA, Kruskal-Wallis, Mann-Whitney test, and Levene statistics using SPSS 18.0 version. Cronbach's α of total (subscales) were 0.955 (0.662-0.909) and 0.959 (0.627-0.919) in physician and nurse, respectively.

Results : The subjects of this study were physician and nurse about twenty and thirty, respectively. Around forty percent of physicians and forty percent of nurses were religious. About sixty percent of physicians and nurses were unmarried. Forty percent of physicians and nurses were on medical unit and sixty were on surgical unit. About half of physicians and forty percent of nurses have experienced the bioethics-related education or seminars. The scores of shared medical decision-making were no differences between physician and nurse groups significantly ($t=1.42$, $p=0.160$), and the score of 'constructing a system' of nurse group was higher than that of physician group ($t=2.44$, $p=0.017$)(Table 1). Total scores of shared medical decision-making according to the responses about 'who should be notified first cancer diagnosis?' were significantly different and the score of 'autonomy' of two groups who responded to 'patients or both of patient and family should be informed of their own diagnosis first' was higher than that of group who responded 'family should be first' significantly ($F=3.38$, $p=0.38$). There were no differences between the three groups in the rest subscales of shared medical decision-making. Total scores of shared medical decision-making according to the responses about 'who should be made final decision in critical situations?' were significantly different ($\chi^2=6.02$, $p=0.049$). Concretely, score of the group who responded to 'final decision-maker is to be patient' was higher than that of group who responded 'physician' significantly. These similar results were showed in subscales 'constructing a system and participation of family'. On the while, autonomy subscale showed that the score of the group who responded to 'final decision-maker is to be physician' was higher than that of group who responded 'patient' significantly. There was showed that the score of 'final decision-maker

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is to be physician, cancer patient, and family in order' at autonomy subscale among all subscales (χ^2=10.80, p=0.005)(Table2).

Conclusion : Currently, changing of the family system and size influenced the individual value system and therefore made impact the decision-making in clinical situations. According to growing rapidly a single person household and young medical staffs, and patients' rights, physicians and nurses responded that final decision-maker should be a patient own in constructing a system, autonomy, and participation of family among the shared medical decision-making.

<Table 1> Differences of Scores of Shared Medical Decision-Making between Medical Staffs

Subscale	Physician (n=50) Mean ±SD	Nurse (n=50) Mean ±SD	t-test	p
1. Sharing information	37.2 ±4.6	38.1 ±4.1	-1.00	(.318)
2. Constructing a system	27.8 ±3.5	29.3 ±2.7	-2.44	(.017)
3. Explanation as a duty	21.3 ±2.4	21.9 ±2.3	-1.15	(.254)
4. Autonomy	16.6 ±2.0	17.3 ±2.1	-1.56	(.122)
5. Capturing time	12.4 ±1.9	12.4 ±1.4	0.12	(.906)
6. Participation of family	12.2 ±1.7	12.6 ±1.8	-1.05	(.296)
7. Human respect	12.1 ±1.8	12.2 ±1.7	- .29	(.776)
Total	139.7 ±14.9	143.7 ±13.3	-1.42	(.160)

Table 1

<Table 2> Shared Medical Decision-Making and Responses of Medical Staffs about Two Questions 'Notifying Cancer Diagnosis & Final Decision-Making'

(doctor 50, nurse 50)

Dependent Variable		No	Mean	±SD	F-test (p)	Mean Rank	x^2-test (p)	Post-hoc Z (p)
<1> Who should be notified first cancer diagnosis?								
Total Score	Patient	19	143.05	13.59	1.34 (.266)	51.37	1.32 (.314)	
	Family	35	138.57	15.43		44.70		
	Patient & Family	46	143.57	13.31		54.55		
4. Autonomy	Patient	19	17.21	2.12	3.38 (.038)	54.26	6.09 (.048)	
	Family	35	16.23	2.18		41.03		
	Patient & Family	46	17.37	1.84		56.15		
<2> Who should be made Final Decision-Making ?								
Total	Patient a)	88	143.14	13.44	4.08 (.020)	53.00	6.02 (.049)	a>c
	Family b)	9	132.78	17.35		35.78		
	Physician c)	3	127.00	11.53		21.33		
1. Sharing information	Patient a)	88	38.04	4.28	3.03 (.053)	52.74	4.71 (.095)	
	Family b)	9	35.11	4.62		36.33		
	Physician c)	3	34.00	3.61		27.17		
2. Constructing a system	Patient a)	88	28.85	2.94	3.65 (.030)	52.61	5.91 (.052)	a>c
	Family b)	9	26.89	4.76		41.72		
	Physician c)	3	25.00	2.00		15.00		
3. Explanation as a duty	Patient a)	88	21.82	2.27	3.96 (.022)	52.85	5.30 (.071)	
	Family b)	9	20.22	2.39		35.56		
	Physician c)	3	19.00	2.65		26.50		
4. Autonomy	Patient a)	88	17.14	1.949	6.98 (.001)	52.76	10.80 (.005)	a>b b<c a<c
	Family b)	9	14.67	2.06		22.28		
	Physician c)	3	18.00	1.73		69.00		
5. Capturing time	Patient a)	88	12.50	1.57	3.45 (.036)	51.57	4.49 (.106)	
	Family b)	9	12.22	2.17		50.94		
	Physician c)	3	10.00	2.0		17.67		
6. Participation of family	Patient a)	88	12.55	1.55	4.57 (.013)	52.15	7.68 (.022)	a>c
	Family b)	9	12.11	2.52		48.61		
	Physician c)	3	9.67	1.53		7.83		
7. Human respect	Patient a)	88	12.24	1.75	.966 (.384)	51.73	1.39 (.500)	
	Family b)	9	11.56	1.59		41.89		
	Physician c)	3	11.33	2.08		40.17		

* 'Constructing a system' was identified to non-homegeneous subscale in Levene Statistic (test of Homogeneity of Variances)

Table 2

PO08-35

EVALUATING THE EFFECTIVENESS OF THE KOREAN PATIENT NAVIGATOR EDUCATION PROGRAM FOR THE NEGLECTED CLASS OF BREAST CANCER

In-Young Han[1*], Jung-Won Lim[2], Young-Sun Rhee[3], Bang-Geul Kang[1], In-Young Moon[1], Ji-Eun Lee[1]

[1] *Dept. of Social Welfare, Ewha Womans Univ., Korea*
[2] *Dept. of Social Welfare, Kangnam Univ., Korea*
[3] *Dept. of Administration and Social Welfare, Chosun Univ., Korea*

Background/Purpose : The purpose of this study is to build up the Korean patient navigator education program for the neglected class of breast cancer and to evaluate its effectiveness.

Methods : During Phase 1, Delphi method was used to build up the Korean patient navigator education program. In Phase 2, the education program was provided to 30 individuals who have willingness to participate in the patient navigator education program and multi-source assessment from learners, instructors, and program managers was conducted to evaluate its effectiveness.

Results : Using a Delphi study, first, the objectives of navigator education program were derived through several themes such as 'Recognize the importance of breast cancer screening', 'Increase the breast cancer screening', 'Identify and remove treatment barriers' and 'Patient's psychological anxiety reduction'. A total of 45 navigator tasks to achieve the objectives were then identified. Moreover, required training subjects, training time, trainer qualification, and training method of performing navigation were identified. After completing our navigator education program, multi-source assessment was conducted. Findings demonstrated that the knowledge of the role of navigators was increased ($t=-2.174$, $p=0.038$). The training and educational goals for learners ($t=-9.001$, $p<0.001$) and instructors (mean=3.96) respectively were also achieved. Based on the results and comments from multi-source assessment, the navigator education program was modified and the final versions of the education program, learners' text book, and the instructor's guidance were made.

Conclusion : The effectiveness of Korean patient navigator education program was demonstrated by multi-source assessment. The effective approach to support the implementation of the navigator training program for the neglected class of breast cancer was suggested.

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INTERCOM Convention Services, Inc.
8th Fl., Samick Lavied'or Bldg., 720-2 Yeoksam 2-dong,
Gangnam-gu, Seoul 135-920, Korea
Tel: +82-2-3452-7291, 501-7065
Fax: +82-2-3452-7292
E-mail: gbcc@intercom.co.kr
Website: www.gbcc.kr

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