Journal of Breast Cancer

The Rainbow of Hope,
Personalized Breast Cancer Care

Global Breast Cancer Conference 2011

GBCC2011

October 6 ~ 8, 2011 Seoul, Korea

ABSTRACT BOOK

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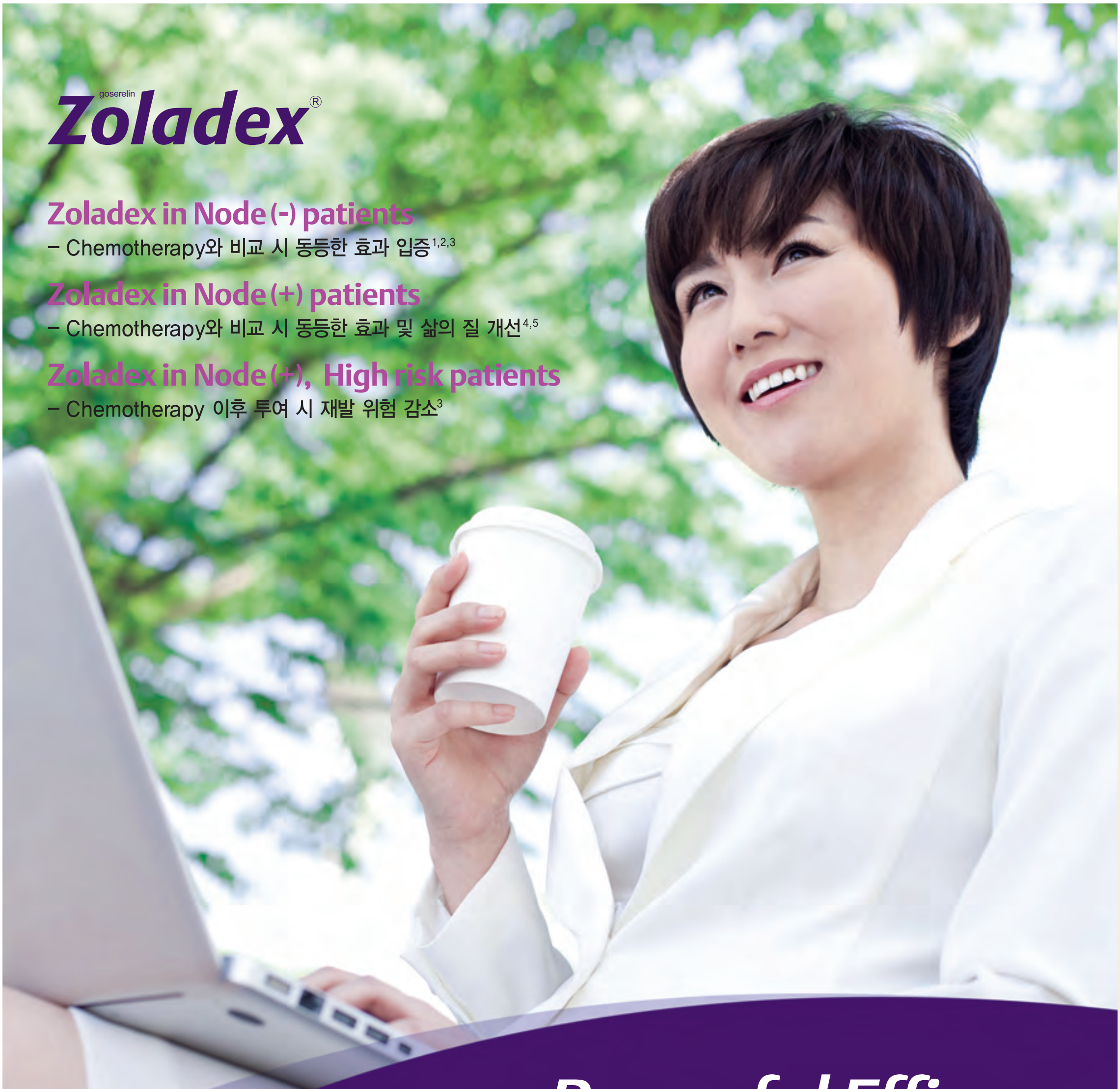
Zoladex®



Zoladex in Node (-) patients

– Chemotherapy와 비교 시 동등한 효과 입증[1,2,3]

Zoladex in Node (+) patients

– Chemotherapy와 비교 시 동등한 효과 및 삶의 질 개선[4,5]

Zoladex in Node (+), High risk patients

– Chemotherapy 이후 투여 시 재발 위험 감소[3]

Powerful Efficacy, Improved QoL[1-5]

Reference 1. Jakesz R et al. ABCSG05, J Clin Oncol 2002;20:4621-4627 2. IBCSG. J Natl Cancer Inst. 2003 Dec 17;95(24):1833-46 3. Baum M et al. ZIPP, Eur J Cancer. 2006 May;42(7):895-904. Epub 2006 Mar 20. 4. H. de Haes et al. ZEBRA QoL. J Clin Oncol 2003;21:4510-4516 5.Kaufmann M et al, ZEBRA, Eur J Cancer. 2003 Aug;39(12):1711-7.

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AstraZeneca ONCOLOGY

Product Information **성분·함량** 1실린지중 : 주성분: 초산고세렐린 (별규) 3.78mg (고세렐린으로서 3.6mg) 부형제: 락타이드/글리콜라이드 공중합체 (별규) 18.0mg **성 상** 1회용 실린지 어프리케이터속에 살균된 백색-크림색의 원주형 데포가 들어있으며 이 속에 초산고세렐린(고세렐린으로서 3.6mg)이 생체내에서 분해되는 매트릭스에 분산되어 있다. **효능·효과** •호르몬요법이 적합한 전립선암 •호르몬요법이 적합한 폐경기전 및 주폐경기 여성의 진행성 유방암 •조기유방암의 보조요법 : 에스트로겐 수용체(ER) 양성인 폐경기전 및 주폐경기 여성의 조기 유방암에 대한 표준 화학 요법의 대체요법 •자궁내막증 •자궁내막조직의 퇴축 : 자궁내막 제거나 절제전에 자궁내막을 얇게 함을 목적으로 투여함 •자궁근종 : 자궁근종을 가진 빈혈환자에서 수술전 철분요법과 병용하여 환자의 혈액상태를 개선함을 목적으로 투여함. •보조생식술 : 배란촉진 과정시 뇌하수체 억제 목적 **용법·용량** 성인 : 고세렐린으로서 3.6mg의 1데포를 28일 간격으로 전방복벽에 피하주사한다. 신장애, 간장애 환자나 고령자의 경우에도 용량을 조절할 필요는 없다. 1. 전립선암, 유방암 : 호르몬요법이 적합한 전립선암 또는 유방암의 관리에 고세렐린으로서 3.6mg 1데포를 28일마다 전방복벽에 피하주사한다. 국소진행 전립선암에 있어서 방사선요법과 병용하는 보조 호르몬요법의 경우 36개월로 사용이 제한된다. 2. 자궁내막증 : 자궁내막증을 이 약으로서 6개월 이상 치료한 임상자료가 없으므로 치료기간은 6개월 이하가 되도록 한다. 뼈 무기질 밀도의 감소 우려가 있으므로 반복적인 치료는 하지 않도록 한다. 이 약 투여시 호르몬 대체요법(에스트로겐 및 프로게스테론 제제)을 병행하면 뼈 무기질 밀도 감소 및 혈관운동성 증상이 감소된다. 3. 자궁내막조직의 퇴축 : 자궁내막의 퇴축을 목적으로 투여할 때는 4주 혹은 8주간 치료한다. 자궁의 크기가 큰 환자에게 투여 시 또는 적당한 수술 일정을 결정하기 위해서 2번째 데포를 투여할 수 있다. 4. 자궁근종 : 자궁근종에 의한 빈혈이 있는 여성에게는 고세렐린으로서 3.6mg에 철분을 보충하여 수술전 3개월까지 투여할 수 있다. 5. 보조생식술 : 에스트라디올 농도가 초기 황체기 수준이(약 150pmol/ℓ) 되도록 뇌하수체를 억제하기 위해 이 약 3.6mg 1데포를 투여한다. 이는 7~21일 사이에 일어난다. 뇌하수체가 억제되면 생식샘자극호르몬(gonadotrophin)으로 배란을 촉진시킨다. 이 약에 의한 뇌하수체 억제는 일정하여 일부 경우, 성선자극호르몬 요구량이 증가될 수 있다. 적당한 시기의 황체기에 성선자극호르몬을 중지하고 사람융모성생식샘자극호르몬(hCG)을 투여하여 배란시킨다. 치료관찰, 난자 회수 및 임신기법은 각 병원의 일반적 방법에 따른다. **사용상의 주의사항** – 이상반응 1) 일반적인 이상반응 : 관절통, 비특이적 감각이상이 보고되었다. 피부 발적이 보고되었으나 일반적으로 경미하게 나타나며 치료를 중단하지 않아도 대부분 사라진다. 때때로 피하 주사 부위에 약한 타박상과 같은 국소반응이 나타날 수 있다. 드물게 과민반응이 보고되었으며 아나필락시가 나타날 수 있다. 동일 계열의 약물들과 같이 매우 드물게 뇌하수체졸중이 초기 투여 후 보고된 바 있다. 2) 순환기계 : 때때로 저혈압 또는 고혈압 등 혈압변화가 관찰되었다. 이 변화는 보통 일시적이며 투여기간 중 또는 투여를 중지하면 회복된다. 드물게 이 변화로 인해 치료를 중지하는 등의 처치가 필요할 수 있다. 3) 남성 : 약리학적 효과로 홍조, 발한, 성욕감퇴, 성교능력 감퇴가 나타나며 드물게 치료를 중단해야 하는 경우도 있다. 드물게 유방압통 및 팽만감이 나타난다. 초기 전립선암 환자의 경우 일시적으로 골통증이 증가할 수 있으나 대증요법으로 완화시킬 수 있다. 요관 폐쇄증과 척수 압박이 별개의 경우로 보고된 바 있다. 뼈 무기질 밀도 감소가 야기될 수 있다. 4) 여성: 홍조, 발한, 성욕변화 등 발현. 드물게 치료중단의 경우 있음. 두통, 우울 등 기분변화, 질건조, 유방크기 변화. 섬유종환자의 경우 퇴행 가능. 전이 유방암 치료 초기 고칼슘혈증 발현. 초기 투여 시 질출혈 나타날 수 있고, 에스트로겐 금단에 의한 것이며 자연히 없어짐. Gonadotrophin과 병용시 난소과자극 증후군 보고. 5) 유방암 : 진행성 유방암에 이 약으로 치료받은 여성의 이상반응 프로필은 자궁내막증에 이 약으로 치료받은 여성과 일치한다. 이 약과 난소절제술을 한 진행성 유방암을 갖는 폐경 전·후의 여성의 대조임상시험에서 두 그룹 모두에게서 아래와 같은 이상반응이 5% 이상 보고되었다. 홍조(이 약 vs 난소절제술 이상반응(%) : 70 vs. 47), 종양 발적(23 vs.4), 구역(11 vs. 7), 부종(5 vs. 0), 권태감/피로/졸음(5 vs. 2), 구토(4 vs. 7). 임상 2 상에서 진행성 유방암을 갖는 폐경 전·후의 여성에게서 홍조(75.9%), 성욕감퇴(47.7%)가 보고되었다. 주사부위의 반응은 드물게 보고되었다.

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Co-Chairman of the GBCC2011, Korea

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Ministry of Health & Welfare, Korea

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Luncheon Symposium: Supported By GSK

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Soo Chin Lee, National Univ. Health System, Singapore

Free Paper VIII: Oncology Nursing

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GBCC2011 Conference Report
Chan Heun Park
Kangbook Samsung Hospital, Korea

Award Ceremony
Byeong Woo Park
Yonsei Univ., Severance Hospital, Korea
Sung-Bae Kim
ASAN Medical Center, Korea

Closing Speech
Dong-Young Noh
Seoul National Univ. Hospital, Korea

POSTER DISCUSSION

October 7, 2011 (Friday)

Publication Only

GBCC 2011 Publication Committee

Se Jeong Oh, Young-Jin Suh, Su-Mi Chung, Heeboong Park, Cheolwan Lim, Joo Hyuk Sohn, Young Up Cho, Kwang Sun Suh, Eun-Hyun Lee, Eunjung Ryu

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GBCC2011

Plenary Lecture

THE CHALLENGE OF BREAST CANCER

Eric P. Winer

Breast Oncology Center, Dana-Farber Cancer Institute, USA

The management of breast cancer remains a clinical challenge. Although significant progress has been made over the past 10-15 years, many patients treated for early stage disease continue to suffer a recurrence. In the United States alone, over 40,000 women die of breast cancer each year, and worldwide it is estimated that there are over 400,000 deaths from the disease. It has become clear that breast cancer is family of diseases or a conglomeration of subtypes, defined either by pathologic features such as grade, hormone receptor status, and HER2 status, or by genomic classifiers. Each of these subtypes has its own natural history, characteristic sensitivity to therapy, recurrence pattern, and set of unresolved challenges. Although stage of disease remains important in predicting the risk of recurrence, the biologic subtype of the disease determines appropriate treatment approaches. This lecture will review the four major clinical subtypes of breast cancer (triple negative, HER2 positive, ER+ high grade, ER+ low grade) and the clinical challenges associated with each of these entities. Promising new approaches will be discussed, and critical areas for future research will be identified.

PL2

MOLECULAR SUB-CLASSIFICATION OF BREAST CANCER IN THE ERA OF PERSONALIZED MEDICINE

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FROM CANCER GENOMICS TO CANCER TREATMENT

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To isolate novel targets for diagnosis (predictive marker for the efficacy of treatment as well as tumor marker) and for treatment of cancer (molecular-targeting drug, cancer vaccine, antibody), we have performed expression profile analysis of clinical cancer materials and selected hundreds of candidate genes by the criteria as follows; (1) gene expressions were transactivated in a large proportion of cancer tissues in comparison with their corresponding normal tissues and (2) expression was not observed or hardly detectable in any important vital organs. The further functional analysis identified dozens of genes that are likely to function as oncogenes in various cancers. The suppression of expression of such genes with siRNA induced cell cycle arrest, apoptosis, or suppression of anchoring-dependent cell growth. From such gene products, we screened 9- or 10-amino acids peptides corresponding to a part of oncoantigens that induce cytotoxic T lymphocytes that would specifically kill cancer cells in an HLA-A restricted manner. We have so far isolated nearly 90 peptides (HLA-A02 or HLA-A24 restricted) derived from about 50 oncoantigens and started translational research using some of them in August, 2006. We are now running various protocols and more than 1,500 cancer patients have been enrolled by the end of July, 2011. The promising clinical outcome of our translational research will be introduced. In addition, to discover genetic polymorphisms associated with clinical outcomes of patients with tamoxifen treatment, we conducted a genome-wide association study (GWAS). We studied a total of 345 Japanese patients with hormone receptor-positive, invasive breast cancer receiving adjuvant tamoxifen monotherapy. In the GWAS, we detected significant associations with recurrence-free survival at 15 single nucleotide polymorphisms (SNPs) on 9 chromosomal loci that satisfied a genome-wide significant threshold (log-rank $p = 2.87 \times 10^{-9}/9.41 \times 10^{-8}$). These findings provide new insights into prediction of the clinical outcomes of breast cancer patients treated with tamoxifen.

GBCC2011

Panel

P01-1

TARGETED THERAPY FOR BREAST CANCER: REVIEWS OF PAST DECADE AND FUTURE CHALLENGE

Ian Krop

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Panel

P01-2

DISCOVERY OF MOLECULAR PREDICTORS AND IDENTIFICATION OF SUBGROUP IN THE ERA OF TARGETED THERAPY

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STATISTICAL DESIGNS OF CLINICAL TRIALS OF TARGET THERAPY

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Advances in breast cancer treatment over the last 30 years mean further advances require strategies for development of agents targeted to specific populations. These agents can be developed as single agents or in combination with other therapeutic agents. First consider the situation where it is of interest to combine a new agent with a chemotherapy backbone but the best backbone to use is unknown. It is assumed that the chemotherapy backbone will not make a major difference with respect to activity but one would like to be protected from choosing a clearly inferior combination of the new agent and chemotherapy backbone. A selection design is an efficient design to use to select the backbone. The selection design provides high probability of selecting the best backbone to move forward with in combination if one of the backbone combinations is better by a specified amount. A related question that can be answered with the selection design is: given a chemotherapy backbone, which agent should be moved forward among many agents in a class of similar compounds. Again, the selection design will not show that one agent is significantly better than the other agents. The selection design will allow one to pick the best agent with high probability if the agent is better than the other agents by a specified amount. The selection design is not appropriate for situations where a chemotherapy backbone and the chemotherapy backbone plus a new agent are being compared. Since the chemotherapy backbone is included in both arms the arm without the experimental agent cannot perform better than the arm with the experimental agent. Therefore, in this type of situation there is a .5 probability of choosing the arm with the experimental agent when in fact the experimental agent is adding no benefit. Now consider the situation where there are many agents to study in combination with a chemotherapy backbone but not all of the agents are of the same class. In order to determine activity a randomized study of each combination to control is needed. One design would be for different sites to study an agent and each site would randomly assign patients to the experimental combination in a 2:1 or 3:1 fashion. All sites would combine the data for the control arm. As the accrual goals for each of the different combinations are met, other agents could take their place in the study. In this study all patients must meet the same eligibility criteria. The benefit of this design is that new combinations are compared

to a control arm in a randomized fashion while the shared control arm allows for more efficient use of data than if each combination had its' own control arm. Three designs that have been discussed in the literature to determine activity of molecularly targeted agents in patients selected by a clinical biomarker are as follows: the biomarker-stratified design, the enrichment design, and the biomarker-strategy design. In the biomarker-stratified design, patients are stratified by biomarker status (positive or negative) and within each stratum are randomized to treatment A (a new experimental agent that is targeted for the biomarker) or to control. In this design the following questions can be answered: 1) Is treatment A better than control for each biomarker strata 2) Overall is treatment A better than control 3) Is the biomarker prognostic or predictive. For the enrichment design, biomarker positive patients are randomized to receive treatment A or control and biomarker negative patients are off study. In this design, it can be determined if the treatment is active for the targeted group of patients. It cannot be determined if the treatment is also active in the biomarker negative subgroup of patients. If the agent were active in the biomarker positive group and there was data to indicate the biomarker negative group might also benefit , activity in the biomarker negative group could be addressed later in another study. If the study were negative, it would not be of interest to study the drug further in either population. This design prevents biomarker negative patients from being exposed to an inactive drug. The final design is the biomarker strategy design where people are randomized to biomarker directed therapy or control. Within the biomarker directed therapy arm patients who are biomarker positive receive treatment A and those who are biomarker negative receive control. The patients who are immediately randomized to control may or may not be assessed for the biomarker. This design can answer the question of whether treatment A is better than control for the biomarker positive patients. The biomarker directed arm can be compared to the control arm to determine whether the strategy is better in the overall population. It can also be determined whether the biomarker is prognostic.

LOCAL THERAPY FOR YOUNG BREAST CANCER PATIENT

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These days, breast cancer is one of the leading cancers of women for the whole world. And it has become the major threat to jeopardize their health. The diagnosis of breast cancer in young patients harbors many challenges. Treatment plans should be considered with genetic testing, infertility, pregnancy and psychosocial issues. Young women with breast cancers generally have a higher propensity of pathologic features associated with more aggressive tumor behavior, such as negative hormonal receptors, poor histologic differentiation grade, and lymphovascular invasion. However, even if these differences are accounted for, young age remains an independent risk factor associated with worse clinical outcome, so to be suggested that the relative improvement in survival among older women and the lack of progress in younger women may be due to age-dependent biologic differences not addressed in detail by now. In real, the risk of dying of breast cancer within 5 years of diagnosis in young women with early breast cancer has well been reported higher than in their older counterparts. Like older women, young women with early stage breast cancer are treated with either local therapy like breast conservation (BCT) or mastectomy. Young women have worse local control rates after BCT, compared with mastectomy. However, there is still controversy as to whether this difference in local control translates into inferior survival after BCT in young breast cancer patients. Survival rates among young women with breast cancer lag behind to that of older women. These findings have led to speculation that mastectomy may be better, yet this remains to be elucidated very clearly. Gene expression profiling that is supposed to be addressed in detail elsewhere provides new insight into biological differences that may account for differences in outcomes. With meticulous attention to safety margins and judicious use of radiation and systemic therapy, BCT remains a safe option for young women with breast cancer. The available data to date do vindicate that young women seem to be at a higher risk of local recurrence (LR) following BCT, and it is evident that failure to complete local control does compromise breast cancer-specific survival. However, whether LR is a auspice of or a reason for poor prognosis in young women remains uncertain. LR can be minimized by careful patient selection, attention to margins, the addition dosage of boost radiotherapy, and appropriate systemic therapy. In the absence

of apparent evidence that mastectomy with or without contralateral prophylactic mastectomy improves survival in young women with breast cancer, I understand that BCT remains a safe and desirable local therapy option.

REPRODUCTIVE AND GYNECOLOGIC ISSUES

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Background: Breast cancer is the most common cancer among women in both developing and developed countries. Incidence of breast cancer is rising in Asian countries, and breast cancer is the most common cancer among Asian women. Korea showed significant mean annual percentage changes (7.9%) during the period 1993-2002, incidence rates increased significantly in Korea during the 10-year period in all age groups. Incidence rates and age-specific incidence curves in Korea exhibited low incidence (31.9%) with slow increases until age 50 year and then a gradual decrease. These estimates are based on data from the National Cancer Center and Korea Central Cancer Registries for Health Statistics for the most recent years available (1993 to 2002). The most rapid rises are seen in developing countries. Increasing trends in developing countries are often considered the result of the westernization of lifestyle, factors such as delayed childbearing, dietary habits and exposure to exogenous estrogen. Although incidence rates are substantially higher for women age 50 and older (375.0 per 100,000 females) compared with women younger than 50 years (42.5 per 100,000 females) in the USA, approximately 23% of breast cancers are diagnosed in women younger than 50 years and 15% occur in those younger than age 45. 23% of women diagnosed with breast cancer are premenopausal, their menstrual status often changes on receiving treatment. As Yong women commonly have distinct concerns and issues compared with older women including inquiries about fertility preservation in young breast cancer patients, menopausal symptoms following chemotherapy, contraception and breast cancer diagnosis and treatment during pregnancy. Further they are more likely than older women to have questions regarding potential side effects of therapy and risk of relapse or a new primary. The purpose of this review was to provide an update on the management of reproductive and Gynecologic issues following breast cancer in young women.

Methods: Literature review of reproductive and gynecologic issues in breast cancer patients was done by providing a brief overview and summary of breast cancer management with reference.

Results: There are a number of issues specific to breast cancer diagnosis in young women: first: Breast cancer is uncommon in young women. Younger women are likely to pres-

ent with more aggressive behavior and a worse prognosis. These clinical difference in prognosis have recently been verified by histologic and biochemical analyses of breast cancer in younger women. Second: Issues of fertility-preserving strategies, contraception and risk of premature menopause following cytotoxic chemotherapy are concerns pressing to the young breast cancer patient. The issue of fertility preservation is more complex than in other cancers with concerns that fertility preservation strategies. Currently, there are no treatment which are guaranteed to preserve fertility. Third: Issues related to a new diagnosis of breast cancer associated with pregnancy bring up a multitude of issues in this vulnerable population. Currently, there is no good evidence that pregnancy appear to be detrimental following breast cancer , but individualized counseling regarding prognosis and risk relapse based on their age and pathological features of the cancer is required before patients can make informed decisions regarding future childbearing. Fourth: Psychosocial issues of sexuality and self-image can warrant interventions in this population.

Conclusion: Survival following breast cancer is improving, increasing numbers of breast cancer survivors are consulted with reproductive specialist and gynecologist with reproductive and Gynecologic issues following breast cancer.

BIOLOGIC FEATURES IN YOUNG BREAST CANCER -THE TREND OF BREAST CANCER INCIDENCE CALCULATED BY NSABP/GAIL MODEL-

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Incidence of Breast cancer was different among regions in the world. The difference might be caused in region specific factors including life style, foods, medical care and level of industrization. In addition, ethnicity was involved in the cancer incidence. The peak age of breast cancer was around 50 years old and more than 52,000 Japanese women were newly diagnosed as the breast cancer in a year. In fact, the international epidemiologic data also demonstrated the incidence of Japanese breast cancer in Osaka was higher in young generation rather than elderly population in the USA. In western countries, older than 60 women had frequently suffered from breast cancer and the incidence had been increasing with aging. Differences in incidence among nations were considered to be related to societal changes occurring under the industrialization. Migration studies from Japan to the USA demonstrated that global variation in incidence caused rather than genetic factors alone. Incidence rates of breast cancer was generally increased in second-generation migrants, and the trends of increase further in third- generation migrants as they became further acculturated. These data suggested that environmental and/or life style factors were important factors of breast cancer risk. In the USA, Gail mode/NSABP model were well known breast cancer risk assessment tool for women. However, this model was designed based on the database in the USA. In this regard, Gail/NSABP model could provide reliable risk of breast cancer for Caucasian living in the North America. The recent result from the Japanese case-control study providing identical risk factors in Japanese women. Based on these epidemiological data, breast cancer risk was considered to be different among ethnicity. In this case-control study conducted in Japan, 5,861 including 3,434 case and 2,427 control samples were eligible and analyzed. The results demonstrated that risk factor of breast cancer in Japanese women was similar to that in Western countries. This difference might result in changing life style of Japanese young women for these years. By the way, the recent trend of breast cancer incidence was similar among Asian countries including Korea and China. In fact, the latest epidemiological data in East Asian were suggesting that Asian women might

have similar risk factors except for their life style related factors. To predict the trend of breast cancer incidence in East Asia, we calculated relative risk of breast cancer in either Japanese or Chinese cohorts by using NSABP/GAIL model. We collected epidemiological information regarding breast cancer risk factors from 328 Japanese breast cancer patients and 272 Chinese breast cancer patients. We analyzed profiles of risk factors and calculated relative risk of both subjects. The Chinese cohort was younger in age at surgery and first birth than the Japanese cohort. Otherwise, the Japanese patients were younger in age at menarche than the Chinese patients. There were no statistical difference in number of children between both cohorts, but incidence of pregnancy was higher in the Chinese cohort. Life time risk and 5 year risk calculated by NSABP/GAIL model were similar in both cohorts and we speculated the incidence of breast cancer in Japan and China could be increased for the coming 5 years. In conclusion, the trend of breast cancer incidence might be depended on time series among similar ethnic population and that speed of life time change might result in different epidemiologic profile among East Asia. Therefore, the peak age may be shift with aging for the following 5 years. However, the relative breast cancer risk may be plateau among East Asia in the future.

CURRENT AND FUTURE ROLES OF PRIMARY CHEMOTHERAPY IN PATIENTS WITH OPERABLE BREAST CANCER

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Primary chemotherapy is the gold standard in the treatment of locally advanced, inoperable breast cancer. Gradually, based on profound evidence, primary chemotherapy has become a standard treatment option for patients with operable disease, who are clear candidates for adjuvant chemotherapy. The idea of preoperative chemotherapy extended to include patients with large but operable early-stage breast cancer was initially for the possibility in some cases of downstaging the primary tumor to avoid mastectomy, and to allow breast-conserving surgery to be done. This approach allows the tumor to be used as a measure of treatment response *in vivo*, i.e., improving surgical options and offers an *in vivo* chemosensitivity testing at the same time. More recently, the possibility has opened up for primary chemotherapy to provide information on the use of clinical, pathological, and molecular endpoints, which can be used as surrogate markers to predict long-term outcome in the adjuvant setting. In addition, the anatomical accessibility of the breast provides the potential for serial biopsies to investigate molecular changes during treatment. The research potential for preoperative therapy is huge and could stand for an important advance in the development of conventional adjuvant treatment options because of its greater efficiency at identifying drug activity. When trying to extrapolate the data generated in these relatively smaller preoperative studies to real clinical benefit, the major concern about this effort is whether there is a specific correlation between reproducibly measured in breast response and distant disease-free survival and overall survival end points. For clinical trials, pathological complete response (pCR) is frequently considered as a surrogate marker for favorable long-term prognosis. However, it is very clear now that using pCR rate as a surrogate endpoint for disease-free survival or overall survival is not suitable in estrogen receptor positive patients, either in HER2 positive or HER2 negative disease. The response to treatment is not necessarily equal between primary macro-tumor and micro-metastatic tumor. In clinical service, clinicians need to consider the routine non-investigational use of preoperative systemic therapy considering the evidence for a benefit using tested and standardized adjuvant regimens. Specifically, the same regimens developed in the

adjuvant setting should be used so that clinicians can be sure they are providing established benefits in disease-free and overall survival. Because the hypothesis that response of primary tumor can allow clinicians in non-research settings to tailor therapy and thereby provide improved outcomes is not confirmed. Clinicians should not adopt the routine off-study use of tailored preoperative therapy for patients with operable breast cancer. Such patients should be treated in clinical trials testing new agents and strategies.

PREDICTING NEOADJUVANT THERAPY RESPONSIVENESS AND RESPONSE EVALUATION

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Neoadjuvant therapy for breast cancer is the important treatment modality of locally advanced breast cancer. When administered before surgery, it may induce the down staging of the tumor, facilitate surgery, and raise the possibility of breast conserving surgery. Recently, endocrine therapy has appeared emerging neoadjuvant option in hormone-receptor (HR) positive breast cancers.

Neoadjuvant therapy also can result in 'in vivo' testing of the therapeutic effect of neoadjuvant therapy, which may help to decide further treatment modality individualized. Sometimes, complete regression of tumor in surgical specimen was observed, which referred to as pathological complete response (pCR). Based on several studies which demonstrated the relevance of pCR to better clinical outcome, the pathologic response after neoadjuvant chemotherapy is now considered as an important prognostic parameter. Breast cancer subtypes based on gene expression profiling differ in biologic characteristics and clinical behavior. Instead of genetic procedure, the IHC of ER, PR and HER2 is commonly used in clinical practice.

Based on these backgrounds, decision for neoadjuvant therapies depend on their intrinsic subtypes. Although there are four or five or more subtypes, currently only three therapeutic categories are considered. Therefore, proper choose of neoadjuvant therapies according to biologic subtypes is needed.

Responsiveness of breast cancer to chemotherapy is highly variable according to HR and HER2 expression, and a pathological complete remission (pCR) is rarely achieved by neoadjuvant chemotherapy in ER+HER2- tumors. Moreover, it has been described that neoadjuvant chemotherapy has a limited effect in hormone receptor (HR)-positive breast cancers in terms of pCR rate. Therefore, the factors which may determine the relevance of chemotherapy need to be defined, particular in HR-positive breast cancers. Thus, evaluation for predicting responsiveness of neoadjuvant therapy also should be considered according to intrinsic subtypes. For example, the basal-like and HER2 positive subtypes of breast cancer are more sensitive to paclitaxel- and doxorubicin-based neoadjuvant chemotherapies than luminal and normal-like tumors. Triple negative breast cancer has been reported that pCR to conventional chemotherapy is closely correlated

with clinical outcomes. However, the needs of neoadjuvant chemotherapy for ER-positive tumor are under consideration. In contrast, HER2-directed therapies are considered at first as a neoadjuvant therapeutic option for patients with HER2-positive breast cancers. Finally, specific gene-expression signatures have also been shown to predict pCR following neoadjuvant chemotherapy with an extremely high overall accuracy, sensitivity, and specificity.

Apart from the breast tumor itself, other factors that may predict response include the number of cycles and type of chemotherapy used, tumor tissue microenvironment, and host response. The latter factors are no doubt important, but the current chemotherapeutic protocols are rather limited and use a very similar type of chemotherapy (anthracycline or taxane based) except for human epidermal growth factor receptor 2 (HER2)-positive patients who also receive trastuzumab, and most patients receive 4-8 cycles before surgical excision. The tumor tissue microenvironments and host response may also be important determinants of chemotherapeutic response but appears to be tightly linked to tumor type itself. On the basis of decades of morphologic data, it is well-known that only a subset of ductal carcinomas shows pathologic complete response to neoadjuvant chemotherapy. Recent gene expression-based studies have shown complete pathologic response in 45% of ERBB2 and basal-like breast carcinomas compared with only 6% in luminal subtype. Furthermore, according to a few recent studies, it has been reported that difference in response rates among HER2-positive tumors with the inclusion of trastuzumab in the neoadjuvant chemotherapy regimen.

Predicting the responsiveness of an individual tumor to neoadjuvant therapy has been a major challenge of breast cancer research. A number of prior studies have examined pathologic markers in biopsies 24 to 48 hours post-therapy. Assessment of apoptosis at 48 hours post chemotherapy may predict for benefit to therapy, but another study has not confirmed this at 24 hours post chemotherapy. Similarly, assessment of Ki67 post-therapy has only weak predictive power, and these studies have not identified a consistent predictor of response to therapy.

In this lecture, therapeutic options of neoadjuvant therapies for each subtype are going to be discussed. Then, the discussion about predicting responsiveness for proper neoadjuvant therapies are going to be followed. The implication of neoadjuvant therapies and its clinical relevance for different subtypes in daily practices and future translational research works will be discussed. In addition, some topics under debate for neoadjuvant therapy are opened for discussion.

PREOPERATIVE THERAPY FOR BREAST CANCER

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The main clinical goals of preoperative therapy in breast cancer include tumor downsizing in locally advanced cancers to facilitate mastectomy, and in operable but non-conservable tumors to facilitate breast conserving surgery. In addition, preoperative therapy for breast cancer provides an ideal in vivo model to study pharmacodynamic effects of drugs and to uncover prognostic or predictive biomarkers. However, despite extensive research to identify such biomarkers in breast cancer, few has found routine clinical application, and physicians today are still relying predominantly on conventional markers such as estrogen receptor and HER2 to determine choice of therapy. In the preoperative setting, combination chemotherapy remains the standard systemic therapy for most patients, although the addition of an anti-HER2 agent is now routine in HER2 positive cancer, and recent preliminary data from phase III randomized studies suggest that combining two anti-HER2 agents may further improve efficacy. In tumors that are strongly hormone receptor positive, endocrine therapy may be used instead in selected cases. Much research has been focused on optimizing therapy in triple negative breast cancers, and conflicting studies have variably suggested taxanes, platinums, bevacizumab, cetuximab, etc, to result in better efficacy, although none has been prospectively validated and no regimen is the accepted standard in this subgroup. With regards to biomarkers to guide the choice of therapeutic agent, many are under investigation but few are used routinely in clinical practice. Promising tumor biomarkers include tumor Ki67, whose baseline levels have been reported to predict chemoresponsiveness and post-chemotherapy levels to correlate with survival. Topoisomerase II amplification or deletion has been shown in several studies and a meta-analysis to predict sensitivity to anthracyclines, while the presence of a truncated HER2 (p95HER2) predicts resistance to trastuzumab and may identify patients who may be more optimally treated with a tyrosine kinase inhibitor such as lapatinib. More recently, a stroma-related gene signature was reported to predict chemotherapy resistance, suggesting role of the tumor microenvironment in mediating treatment response. In addition to tumor biomarkers, there has been extensive research to identify germline variants that influence drug outcomes (pharmacogenetics), although only a few, e.g., DPD and 5-fluororuracil, have been incorporated into drug labels in cancer. Several promising germline variants have been reported to predict pharmacokinetics and/or pharmacodynamics of commonly used breast

cancer drugs, including anthracyclines, taxanes, tamoxifen, and aromatase inhibitors, but await prospective validation. Disappointingly, the promising correlation between CYP2D6 genetic variants and tamoxifen outcome from smaller retrospective studies failed to be replicated in two large phase III studies, highlighting the importance of rigorous validation in large datasets. Finally, the existence of inter-ethnic difference in pharmacogenetics could result in inter-population difference in drug outcomes. For example, a CBR3 variant common in Chinese but rare in Caucasians was associated with slower inactivation of doxorubicin resulting in more severe hematologic toxicity, and may account for the greater doxorubicin-induced myelosuppression observed in Chinese than Caucasians. More recently, the UGT2B17*2 deletion variant was reported to significantly reduce the metabolism of exemestane in vitro. This variant is common in Asians (60-70%) but rare in Caucasians (< 10%) and may cause inter-ethnic difference in outcome to exemestane. Asian physicians should be mindful of these differences that may have clinical relevance to their patients.

NEW POWERFUL MOLECULAR ANALYTICAL TOOLS FOR TRANSLATIONAL RESEARCH- A TECHNICAL REVIEW

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According to evolution of high throughput molecular analysis technologies, translational research face challenges to determine proper methodologies that are fit for study purpose because each technology has different assay capability of the accuracy, robustness and reproducibility. This presentation will review three categorized molecular analytic tools (Gene expression profiling, DNA mutation profiling and protein expression profiling of circulating tumor cell [CTC]) based on NSABP pathology lab experience. Gene expression profiling tools are important to identify context oriented specific target genes. Affymetrix genechip assay, Agilent microarray assay and ilumina Whole-Genome DASL assay have their unique assay chemistry and hybridization characteristics. Comparing each whole genome microarray assay performance in paraffin embedded formalin fixed tissue with large number assay cases will help future choice of microarray format for translational study. As a gene expression validation assay and clinically adaptable test, Teqman RT-PCR assay and nCounter assay are examined their sensitivity and agreement to microarray data. Some well known oncogenes and tumor suppress genes are suggested a relevant prognostic and predictive markers. DNA mutation profiling using Mass Spectrometry with iplex chemistry which is a medium throughput mutation screening tool shows high sensitivity and specificity in predefined important genes. Not only the simple enumeration of CTCs but also their individual cell molecular characterization provides a chance to demonstrating their cellular discrepancy from primary and metastatic tumors, and it also give clues to their molecular characteristics are changed during the course of specific cancer treatment. ImageStreamX assay that characterize individual circulating tumor cells protein expression phenotype with high quality image and sensitivity. We can see potential usefulness of ImageStreamX assay in CTC study. Each technology has pros and cons technical limitation. Understanding of technology of tools and using proper tool will give a chance to save time and effort in translational research.

P04-2

EFFORTS OF TRANSLATIONAL RESEARCH IN LAST DECADE: DISCOVERY OF GENE EXPRESSION SIGNATURES FOR PROGNOSTICATION AND PREDICTION

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Breast cancer is a complex and heterogeneous disease. Over the last decade, gene expression profiling has contributed significantly to our better understanding of this heterogeneity at the molecular level. This has led to the refining of breast cancer taxonomy initially based on simple histological features such as histological type, tumour size, tumour grade, lymph node status and the presence of predictive markers such as estrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER-2), to a more sophisticated classification of luminal A, luminal B, HER-2 positive, basal-like and the normal subtypes.

While enormous efforts have been put forth in translational breast cancer research, the disclosure of the entire human DNA sequence has enabled our identification of various driver genes, and the core cancer pathways. The genetic molecular profiling has helped us identified prognostic patterns for breast cancer while a high-throughput mutation profiling platform has been developed to query a large panel of critical cancer gene mutations. Breast cancer translational research has indeed improved our understanding of the biology of breast cancer, leading to discoveries of novel detection approaches, effective therapeutic strategies, and the breakthroughs from bench to bedside. These include bringing personalized management of breast cancer into reality with the advent of the intrinsic classification by Dr. C.M. Perou and his team in 2000, leading to our ability to target cancer interventions to individuals who will benefit most and yet sparing the unnecessary risks and costs to those who will derive little benefit or even be harmed.

Various gene expression profiling approaches have been used to develop genomic tests that may provide better predictions of clinical outcome than the traditional clinical and pathological standards. These include the use of the 70-gene microarray prognosis profile (MammaPrint) in a randomized trial of breast cancer patients, confirming that the microarray test could save up to 30% of breast cancer patients from undergoing unnecessary chemotherapy, and could identify 5% of patients who are undertreated. Another molecular molecular assay, Oncotype DX, exemplifies the candidate-gene approach to

estimate outcome by measuring the expression of ER and HER-2 as well as that of ER-regulated transcripts and several proliferation-related genes, with the use of quantitative reverse-transcriptase-polymerase chain-reaction (RT-PCR) assay. Moreover, the Investigation of Serial Studies to Predict Your (I-SPY TRIAL) also attempts to use biomarkers to identify agents that are effective in specific subpopulations of breast cancer patients. A meta-analysis of publicly available gene-expression and clinical data from almost 3000 breast tumours has supportive the relationship between the risk of recurrence and the breast cancer molecular subtypes, including several different signatures as well as routine clinical and pathological variables. An encouraging finding is that all evaluated signatures showed similar performance despite the limited overlap of genes.
However, the discovery of these various gene expression signatures has posed several practical challenges with theoretical limits to the accuracy of any response predictor that measures the characteristics of only the cancer, the unpredictability of the host characteristics such as the rate of drug metabolism, the considerable uncertainty as to what level of predictive accuracy would be clinically useful as different levels of accuracy may be required for different individual clinical situations, and the quest for comprehensive prospective data. In response to this, there has been an emerging trend of many studies of genomic markers focusing on neoadjuvant treatment of breast cancer. With neoadjuvant treatment aiming at reducing mortality and improving surgical options for breast cancer patients, this offers an in vivo chemosensitivity testing at the same time, being the ideal setting for clinical and translational research. Most of the clinical trials examining the correlation between complete pathological response and long-term cancer-free survival have reported a strong association between the two outcomes.
Furthermore, the tissue specificity nature and relative stability of miRNA has led to significant interest in the exploration of miRNA as potential cancer biomarkers for diagnosis and prognosis. The discoveries of various oncogenes, tumour suppression genes, tumour angiogenesis, cancer stem cells etc. has also led to the exposure of complexity of breast cancer. While a number of targeted agents have been developed in recent years, efforts have been made to identify further biomarkers for tumour response prediction of targeted agents, indicating personalized medicine is steadily emerging as the new treatment paradigm for breast cancer.
Translational breasts cancer research has indeed emerged as one of the hot-off-the-press in the 21st century. This lecture will give an overview of the development of translational research in breast cancer, demonstrating the important discoveries of molecular, clinical and therapeutic research findings in the last decade, the clinical applications and new approaches propelling the translation of bench discoveries into the most optimal bedside management.

P04-3

NANOMEDICINE IN BREAST CANCER DIAGNOSIS AND TREATMENT: VISUALIZATION OF MOLECULAR PATHWAYS AND QUANTIFICATION OF HER2 PROTEIN BY FLUORESCENT-LABELED ANTIBODY

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Nanomedicine is generating a new wave of drug delivery strategies in cancer therapy. With bright and photostable fluorescent nano-particles, quantum dots (QDs), we have developed an optical system to image a single molecule in vivo with a spatial precision of 9 nm in tumor-bearing mice implanted with human breast cancer cells. Our previous studies succeeded in tracking anticancer drug Trastuzumab (anti-HER2 antibody) conjugated with QDs in tumor-bearing mice (Biochem Biophys Res Commun 2006; Cancer Res 2007; Brest Cancer Res 2009). We identified six processes of Trastuzumab delivery: initially in circulation within a blood vessel, during extravasation, in interstitial tissues of extracelullar region, binding to HER2 on cancer cell membrane, moving from cell membrane to perinuclear, and in nuclear regions, with quantitatively-analyzing processes to understand rate-limiting constraints on drug delivery. The movement of Trastuzumab-QDs at each stage was "stop-and-go." Especially, it was interesting that Trastuzumab bound HER2 on cancer cell membrane was internalized by endocytosis and endocytotic vesicles including Trastuzumab-QDs were transported from cell membrane to perinuclear region in vivo. Thus, image analysis of delivery processes of single particles in vivo provides valuable information on antibody-conjugated therapeutic nanoparticles, which will be useful to increase therapeutic efficacy. To understand mechanisms of caner metastasis, we further developed a method to image a cell membrane protein in metastatic cancer cells with antibody-conjugated QDs. A metastasis-promoting factor on cell membrane, protease-activated receptor 1 (PAR1), was labeled with QDs conjugated with anti-PAR1 antibody. Movements of cancer cells and PAR1 during metastasis were clearly observed in vivo. Images of PAR1 dynamics were taken of cells representative of four-stage metastasis; i.e., cancer cells far from blood vessels, near vessel, in bloodstream, and adherent to inner vascular surface in normal tissues near tumor were photographed. These locations represent the process of cancer

metastasis. The diffusion speed of PAR1 in static cells far from tumor blood vessels was slow, but was much faster for moving cells near vessels and in bloodstream. The diffusion speed of cells adhering to inner vascular surface in normal tissues was significantly reduced. Cells formed invadopodia- and lamellipodia-like structures during migration. The diffusion speed of PAR1 on these pseudopodia was faster than in other membrane regions in the same cell. In conclusion, membrane fluidity of metastasizing tumor cells increases during intravasation, reaches a peak in vessel, decreases during extravasation, and is higher in locally formed pseudopodia (J Biol Chem 2010). The dramatic changes in membrane fluidity and morphology enable cancer cells to metastasize. Another progress is an application of nano-biotechnology to quantitatively evaluate amount of cancer-related protein, such as HER2. Now, we face two problems in evaluation of HER2 expression level, 1) the difference of epitope between Trastuzumab and diagnostic anti-HER2 antibody (HercepTest) and 2) the discordance between IHC and FISH data. Therefore, we have developed a quantitative assay using fluorescent-labeled Trastuzumab as a diagnostic probe to directly assess indication of target-oriented therapy for breast cancer patients. The 21st century would become an era when conventional qualitative or analog pathology shifts to quantitative or digital pathology when such nano-biotechnology would be utilized. We expect that our present studies using nanotechnology bring some lights on improvement of drug delivery system, mechanism of cancer metastasis, and develop quantitative pathological diagnosis, with opening new avenues for cancer diagnosis and treatment.

P04-4

STATISTICAL DESIGN OF CLINICAL TRIALS

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Phase II/III, seamless phase II/III, and integrated II/III designs are terms that are used interchangeably and refer to study designs that combine aspects of phase II drug development and aspects of phase III drug development into one study. Phase II/III designs randomize patients in the phase II component and then include these patients in the phase III component of the study. An intermediate end point is evaluated in the phase II component. The elements of a phase II/III design are as follows. The overall sample size (total number of patients) is calculated based on the phase III endpoint. The phase II component of the study can be viewed as an interim futility analysis with an intermediate endpoint. That is, patients are accrued to the study until a specified number of patients are on study. At that point an analysis based on an intermediate endpoint is performed. If a pre-specified activity criterion is met, accrual is continued to the study until the overall sample size is met. All patients are then used in the phase III analysis (final analysis). Challenges in designing phase II/III studies are the choice of the intermediate endpoint (or phase II endpoint), the decision criterion for stopping, and timing of the interim analysis. The intermediate endpoint should be related to the primary endpoint in such a way that at a minimum, lack of effect on the intermediate endpoint is a reliable indication of there being no an effect on the primary endpoint. (This is the standard assumption that has historically been made when using PFS or response rate in single arm phase II studies or randomized phase II studies.) The intermediate outcome should be observed earlier than the primary endpoint. If the intermediate endpoint is obtained late (or at a time that is not much different than the primary endpoint) then the benefit of the interim analysis (or the chance to stop the study early and save patients entering onto the study) will be lost. The stopping criterion should be such that there is a high probability of stopping the study under the null hypothesis while having little impact on the overall power of the study to detect a true benefit on the primary endpoint. The timing of the interim analysis should be such that if the regimen is inactive the study will stop as early as possible during accrual but late enough so that a reliable decision can be made. For example a phase II/III study in Breast Cancer maybe desirable in a metastatic triple negative population where it is of interest to combine a new agent with known chemotherapy agents. In the past metastatic breast cancer studies were used to determine activity in order to move agents into an earlier stage population. Currently interest lies in

developing agents to extend survival in the metastatic population. This means that metastatic patients will be used to provide activity data as well as determine if the agent extends survival. Obtaining activity data often requires a randomized phase II study with a control arm. A randomized phase II study is needed instead of a single arm study since it is difficult to interpret whether the median progression free survival or response rate has increased because of the addition of a new agent to an active regimen without a comparison to the active regimen. If the activity bar is met than a phase III study with the same arms would be of interest using overall survival as the primary endpoint. The II/III design can also be useful in the early stage breast cancer setting by using neoadjuvant (pre-operative) therapy. Here, pathological complete response (pCR) rate could be used as the intermediate endpoint to determine activity in the phase II setting. If activity was shown the study would continue to the phase III phase with DFS as the primary end point. Patients from the phase II study would be used in the phase III study resulting in a more efficient use of patients.

P05-1

PROGNOSTIC AND PREDICTIVE MARKERS IN BREAST CANCER

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The traditional approach in treating human cancer has been largely empiric. This inefficient practice of "one size fits all" invariably leads to inappropriate therapy and treatment-related toxicity in a not insignificant number of patients. Some patients with aggressive disease may be undertreated while others with indolent disease may be overtreated. For those receiving therapy, only a subset of such patients will clinically benefit while adverse side effects commonly affect most if not all patients. Furthermore, severe and sometimes fatal toxic effects will afflict a minority of these treated patients.

Due to the recent developments of gene sequencing, targeted therapies, and molecular diagnostics, cancer treatment has moved towards a personalized approach where treatment is tailored to a given patient (i.e. the correct drug at the correct dosage to the patient who is most likely to derive clinical benefit). To this end, the identification and use of prognostic and predictive markers are critically important. Furthermore, earlier diagnosis of breast cancer is increasingly prevalent due to improved imaging methods and screening programs which only further underscores the need for these markers to quantify the residual risk of patients and to indicate the potential value of additional treatment strategies.

Both prognostic and predictive markers are important in the process of individualizing treatment but they have distinct roles. Both may be derived from either the characteristics of the patient and/or the tumor. Many factors have mixed prognostic and predictive significance.

Prognostic markers consists of traditional factors including clinical and pathologic criteria as well as newer, biologic markers (or biomarkers). Prognostic markers have traditionally been defined as factors that predict disease outcome in the absence of systemic therapy. Recently, this definition has been modified to also include factors that predict an outcome different from that of patients without the marker, despite empiric therapy. Ideally, a prognostic marker should help classify patients into subgroups for which dif-

ferent treatment options, including the possibility of foregoing treatment entirely, can be made. Conventional prognostic factors for breast cancer include the patient's age, tumor size, tumor grade, and extent of axillary lymph nodes involved by metastatic carcinoma. A tremendous amount of research has been performed to identify biomarkers that can serve as additional prognostic markers. Biomarkers provide prognostic information that is either additional or independent of conventional prognostic factors, stronger than conventional prognostic factors or specific to a patient subgroup defined by traditional criteria (i.e. lymph node-negative breast cancer).

Different from prognostic markers, predictive factors guide the choice of treatment. In simplest terms, patients who are found to have certain serum or tissue-based marker level/positivity that suggests clinical response to a specific therapy are clearly the ones who are candidates for that treatment. Conversely, these factors will identify patients who are unlikely to show response to a specific therapy and such information will help redirect the treatment regimen in these patients.

The use of a particular biomarker for prognostic and/or predictive purposes requires the existence of a technically validated, robust, standardized and cost-effective assay to measure it. These can either be serum-based or tissue-based markers. Tissue-based prognostic biomarkers can be assessed by immunohistochemistry (HER-2), fluorescent *in situ* hybridization (FISH) (HER-2), and multigene signatures by gene expression microarray (Mammaprint) or multiplex PCR (Oncotype DX). Three well-established tissue-based predictive biomarkers Estrogen Receptor (ER), Progesterone Receptor (PR) and HER-2 are currently employed in daily practice. ER and PR are used to identify patients eligible for endocrine therapy (tamoxifen and aromatase inhibitors). HER-2 is used for identifying patients likely to respond to specific anti-HER-2 therapies (trastuzumab). Emerging biomarkers such as Ki-67 also show promise for the future.

P05-2

PROMISE OF NEW DEVELOPING PRECLINICAL BIOMARKERS

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Breast cancer treatment has experienced several changes in the past decades due to the discovery of specific prognostic and predictive biomarkers that enable the application of more individualized therapies to different molecular subgroups. Now, there is an urgent need for blood-based, noninvasive molecular tests to assist in the detection and diagnosis of cancers in a cost-effective manner at an early stage, when curative interventions are still possible. Additionally, blood-based diagnostics can classify tumors into distinct molecular subtypes and monitor disease relapse and response to treatment. Increasingly, biomarker strategies are becoming critical to identify a specific patient subpopulation that is likely to respond to a new therapeutic agent. The improved understanding of the underlying molecular features of breast cancer and the availability of a multitude of recently developed technologies including proteomics and genomics have made it possible to develop clinically applicable and cost-effective tests. Circulating micro-RNA and circulating tumor cells are also promising biomarker for the early detection of breast cancer. Overall, the paradigm shift towards personalized and individualized medicine relies heavily on the increased use of diagnostic biomarkers and classifiers to improve diagnosis, management and treatment. Careful randomized prospective testing and comparison with existing established factors will be required to select those emerging markers that offer substantial cost-effective benefit and thereby justify their routine use for breast cancer therapy decision-making. Here, I review the recent technological and scientific advances in this field and will introduce our experiences.

EMERGING BIOMARKERS IN NEOADJUVANT ENDOCRINE THERAPY

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A key objective for oncologists is to find a method of assessing novel Biological Therapies in breast cancer without the need for extensive phase 3 studies. We have, over the past years, developed tools to assess response. These take the form of two distinct pharmaco-dynamic tests: (a) Immunohistochemical and enzymatic assessment of tissue following a short course of novel therapy; and (b) PET scanning using FDG/FLT/11C Choline In terms of immunohistochemistry, aside from Ki67, we have examined phosphorylated ER (PS118), phospho-EGFR, as well as FOXM-1, FOXO3a, Phospho-Akt, Phospho-MAP Kinase. Sample handling and equivalence is critical, since, particularly with phosphorylated epitopes, this can affect results. In this context, we have examined the effects of placebo, genfitinib and; apatinib. PET scanning avoids the issues of sample handling and heterogeneity. Over the past 5 years, we have evaluated PET scanning for its role in assessing early response to therapy, as well as the correlation with MAPKinase and Ki67. Further, early results suggest that 11C Choline uptake can give a good indication of Trastuzumab effectiveness. Together, it is hoped that these newer pharaco-dynamic measures may help in selecting new therapies for ER positive breast cancer, thus obviating the need for extensive multi-centre studies of heterogeneous patient populations.

P06-1

UNDERSTANDING THE BREAST CANCER STEM CELLS: NOVEL PARADIGM FOR CANCER TREATMENT

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Breast cancer heterogeneity can be explained by either cancer stem cell theory or clonal evolution hypothesis. Recent studies indicate that breast cancer stem cells are highly tumorigenic and are responsible for treatment resistance and recurrence of tumors. However, the methodological definition of cancer stem cell is still controversial since there are no widely-accepted surface markers of breast cancer stem cell. Also, most studies have focused on the observations from experiments using selection process with surface markers. Establishing a highly tumorigenic primary breast tumor cell line with stem cell phenotype can be helpful in investigating the biology of breast cancer stem cell. In our laboratory, we have established a breast cancer cell line that is highly aggressive, and resistant to standard systemic treatment. We isolated long-term self-renewing sarcospheres (designated NDY-1) from primary breast carcinosarcoma tissue (sarcoma component >95%) using the anchorage-independent culture method. NDY-1 spheres expressed various mesenchymal cell markers, and their tumorigenic potential was markedly reduced in adherent culture conditions, compared to spheres. Screening for integrins revealed a marked decrease in CD49d expression in adherent culture conditions of NDY-1. The CD49d+/high subpopulation sorted from NDY-1 spheres displayed higher cell viability and sphere-forming ability than CD49d-/low population in vitro. Moreover, the CD49d+/high population displayed high tumor initiating ability in limiting dilution transplantation to NOD/SCID mice, and the xenotransplanted CD49dhigh/+ population recapitulated the complexity of the original primary tumors. Greater doxorubicin resistance was exhibited by the CD49d+/high population, compared with the CD49d-/low population. Thus, our results collectively demonstrate that CD49d+/high cells from sarcospheres display enhanced sphere-forming, drug resistance and tumor-initiating abilities. Additionally, we are now investigating various novel pharmaceutical agents in regard to their ability to affect the growth of breast cancer stem cell population. Recently, we are focusing on the role of various salt types of metformin in breast cancer cell lines and our preliminary data shows promising results on the role of metformin in reducing stem cell-like populations and reversing treatment resistance.

UNDERSTANDING THE CIRCULATING TUMOR CELLS

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P06-3

THERAPIES TARGETING CANCER STEM CELL

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Although breast cancer stem cell was identified ten years ago, investigational new targeting drug has not been developed until now. Breast stem cell could be similar characteristics to breast cancer stem cell, therefore, drugs targeting breast cancer stem cell might also damage breast stem cell. During ten years, many scientists focused on mechanism of stemness and differentiation signals. However, these approach could not overcome such limitations.

Among new drugs, a notch signaling pathway (gamma secretase) inhibitor (MK-0752, Merk) has been tried a couple of trials (phase I/II), but these trials are not recruiting now. Excluding MK-0752, there is not any new targeting drug to breast cancer stem cell in the clinical trial level.

Only several agents (salinomycin, sulforaphane, metformin) have been studied under preclinical trials and early phase I/II clinical trials. I hope to address and review past and present of these drugs and also present my researches.

Gupta et al implemented a chemical screen and discovered compounds showing selective toxicity for breast cancer stem cell. One compound, salinomycin, reduces the proportion of breast cancer stem cells by > 100-fold relative to paclitaxel, a commonly used breast cancer chemotherapeutic drug. Treatment of mice with salinomycin inhibits mammary tumor growth in vivo and induces increased epithelial differentiation of tumor cells. The exact mechanism of salinomycin-induced apoptosis remain unclear, but it appears that salinomycin activates an unconventional pathway of apoptosis that may contribute to the breakdown of apoptosis resistance in cancer cells. However, human toxicities were not studied until now, therefore it should be undertaken clinical studies using salinomycin. Our study also showed that mouse mammary epithelial cell inhibited by salinomycin in MTT assay and mammosphere culture in terms of mammosphere size and number.

Metformin increases skeletal muscle glucose uptake and reduces hyperglycemia plus hyperinsulinemia and may have insulin-independent effects through stimulation of the AMPK. Therefore, metformin has been used as a major anti-diabetic drug. Hirsch et al showed that low doses of metformin, a standard drug for diabetes, inhibits cellular transformation and selectively kills cancer stem cells in four genetically different types of breast cancer. The combination of metformin and doxorubicin, kills both cancer stem cells and

non-stem cancer cells in culture. Furthermore, this combination therapy reduces tumor mass and prevents relapse much more effectively than either drug alone in a xenograft mouse model.

Sulforaphane was found to be converted from glucoraphanin, a major glucosinolate in broccoli/broccoli spouts. Le et al reported that sulforaphane decreased aldehyde dehydrogenase-positive cell population by 65% to 80% in human breast cancer cells and reduced the size and number of primary mammosphere by 8- to 125-fold and 45% to 75%, respectively. Daily injection with 50 mg/kg sulforaphane for 2 weeks reduced aldehyde dehydrogenase-positive cells by >50% in nonobese diabetic/severe combined immunodeficient xenograft tumors. Sulforaphane eliminated breast cancer stem cells in vivo, therefore abrogating tumor growth after the reimplantation of primary tumor cells into the secondary mice. Our laboratory showed similar in vitro data using mouse stem cell rich-mammary epithelial cell.

Although, several candidate drugs have been tried in vitro level and in vivo level, these drugs need more clinical validation and more exact verification of the mechanism.

P07-1

A DOUBLE-EDGED SWORD, AROMATASE INHIBITOR; LET'S TAKE ACTION ON BONE, NOW!

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Advances in adjuvant therapy have led to improvements in the long-term survival of women with early breast cancer (EBC); the 10-year probability of survival is now 90%. The effectiveness of aromatase inhibitors (AIs) on disease free survival in endocrine-responsive EBC is well known. The AIs such as anastrozole, letrozole, and exemestane are significantly more effective than the selective estrogen-receptor modulator (SERM) in preventing recurrence in endocrine-responsive EBC. AIs are likely to replace SERMs as first-line adjuvant therapy for many patients. Meanwhile, the use of AIs increases bone turnover and induces bone loss at sites rich in trabecular bone at an average rate of 1-3% per year leading to an increase in fracture incidence compared to that seen during tamoxifen use. The use of anastrozole had deleterious effect on spinal bone mineral density (BMD) in postmenopausal women with EBC by 2.2% loss in 1 year and 7-8% over the 5 years in ATAC [Anastrozole, Tamoxifen, Alone or in Combination] trial. The incidence of all fractures in the 2007 update was 12% in the anastrozole group and 7.5% in the tamoxifen group. In the BIG [Breast International] 1-98 study of studying effect of letrozole over tamoxifen, a 50% excess of fractures was observed with a median follow-up of 30 months concordant with significant bone loss both in spine and hip. As antiresorptive agents, oral and intravenous bisphosphonates such as alendronate, risedronate, ibandronate, pamidronate, and zoledronic acid have efficacy in preventing postmenopausal osteoporosis, cancer treatment-related bone loss, or skeletal complications of metastatic disease. Administration of immediate zoledronic acid in the postmenopausal women with EBC starting with AI significantly prevented bone loss in the Zometa-Femara Adjuvant Synergy Trials (Z-FAST [US])/(ZO-FAST [Europe]). Studies with a number of oral bisphosphonates, such as anastrozole and risedronate in the SABRE [The Study of Anastrozole with the Bisphosphonate RisedronatE] trial, and anastrozole and ibandronate in the ARIBON trial have also shown effectiveness of bisphosphonates in preventing or treating AI-induced bone loss. We have also recently demonstrated that administration of 24 weeks of a combinative agent of 5 mg alendronate and 0.5 μg calcitriol is quite effective in preventing spinal bone loss in patients with Korean EBC starting

AI. Current clinical practice guidelines recommend baseline and annual follow-up bone density monitoring for all patients initiating AI therapy. Bisphosphonate therapy should be prescribed for patients with osteoporosis and considered on an individual basis for those with osteopenia. Adequate calcium and vitamin D intake, weight-bearing exercise, and smoking cessation should be emphasized in all patients with EBC receiving AI. In conclusion, in postmenopausal women who are receiving AI for EBC, the proper use of bisphosphonate will help prevent further bone loss and occurrence of fragility fractures.

P07-2

LONG-TERM SURVIVORSHIP WITH THE PATIENT'S VIEW, SUPPORTING SYSTEM

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Background: A two-week intensive training program was offered by the Cancer Club in Shanghai, China to improve the quality of life among breast cancer survivors. The training program included three main aspects: understanding treatment options, building relationships among members for support, and coping with stress. Participants checked into the dormitory at the Cancer Club and spent two weeks living together as a group during the training. Although the Cancer Club has been offering cancer support groups as well as training programs for the past fifteen years, this evaluation project is the first one conducted with a community participatory approach.

Methods: Two focus groups were conducted before and after the intensive training to assess the reasons for participating in this training program and how they view their quality of life before and after the training. A total of thirty participants were included. All the participants were female and diagnosed with different stages of breast cancer. The contents of the focus group discussion were recorded in Chinese and the PI of the project analyzed the data with the assistance of a faculty from a local university, two research assistants, and the Director of the Cancer Club.

Results: Preliminary qualitative results indicated a positive response to participating in the training. Overall quality of life was reported to have improved. Although it was not the intent of the intervention, participants reported their main reason to enroll in the training was to prevent the recurrence of breast cancer. Most participants reported that they experienced extreme stressors before they were diagnosed with breast cancer and hoped to learn how to cope better with stressors.

Conclusion: Overall the training is considered to have achieved the three objectives. The success of this program also includes several significant cultural reasons. First, due to an early retirement age of 50, most women are not employed and have the time to participate in such an intensive training. Second, living in a metropolitan city like Shanghai, participants are more aware of the value of breast cancer screenings and preven-

tion. Judging from the responses of the participants, qualitative research methods such as a focus group is considered as a culturally appropriate approach to conducting program evaluation.

P07-3

INDIVIDUALIZED POSTOPERATIVE FOLLOW-UP BASED ON THE KI-67 INDEX FOR THE RISK OF RELAPSE AND RECURRENCE TIME FOR BREAST CANCER PATIENTS

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Background: The American Society of Clinical Oncology (ASCO) guidelines recommend careful history taking, physical examination and regular mammography for appropriate detection of recurrence in postoperative follow-up of breast cancer patients. However, the surveillance programs are uniformly designed. Early (< 2 years) or late (> 10 years) recurrences are often experienced in patients with different characteristics. Moreover, the recurrence profile is different according to tumor biology. In this study, the clinical significance of Ki-67 index as a prognostic marker and as a predictor of recurrence time was evaluated.

Methods: We evaluated 4,133 consecutive patients with primary breast cancer using the Ki-67 index. Out of these patients, 3,190 cases were evaluated simultaneously for estrogen receptor (ER), progesterone receptor (PgR) and HER2 from 1997. The median Ki-67 value was 20%, and cases were divided into 3 index groups; < 20%, ≥ 20% and ≥ 50%. The factors investigated included the presence or absence of lymph node metastasis, nuclear grade, ER/PgR status, HER2 and p53 overexpression. In this study, hormone receptor (HR)-positive and HER2-negative tumors were classified as luminal A type; HR-positive and HER2-positive tumors (HER2 IHC: 3+ or 2+ and FISH amplification ratio > 2.0) as luminal B type; HR-negative and HER2-positive tumors as HER2 disease; and HR-negative and HER2-negative tumors as triple negative (TN) type. Correlations between Ki-67 index and disease-free survival (DFS), overall survival (OS) and recurrence profile such as recurrence time and metastatic sites were investigated.

Results: 1) Ki-67 index and clinicopathological factors. A higher Ki-67 index significantly correlated with larger tumors, younger age, positive lymph nodes, a higher nucle-

ar grade, negative ER/PgR, p53 overexpression and positive HER2. Older patients (≥ 65 years) had tumors with lower proliferation; however, there was no difference in the Ki-67 index values of the tumors in patients between 36-50 and 50-65 years of age. 2) Ki-67 index and breast cancer subtype(s) The median Ki-67 index of tumors with luminal A was 17%, and that of luminal B type tumors was 29%. The Ki-67 index of HER2 tumors was 40% and that of triple negative tumors was 50%. Approximately 60% of the luminal A type tumors had lower proliferation (Ki-67 < 20%), while more than half of the TN type tumors had higher proliferation (Ki-67 ≥ 50%). 3) Ki-67 index and prognosis Patients with a higher Ki-67 index had significantly lower DFS and OS rates. Moreover, the disease-free interval times in recurrent cases were inversely associated with the Ki-67 index. Most of the patients with a Ki-67 index of ≥ 50% had recurrence within 2 years. On the other hand, some patients with a Ki-67 index of < 20% had recurrences over 10 years. Regarding recurrence sites, patients with low proliferation frequently developed bone metastasis; however, diffuse skin recurrence and brain metastasis were often seen in cases with high proliferation.

Conclusion: A higher Ki-67 index correlated with a poorer prognosis and early recurrence, whereas a lower Ki-67 index correlated with a favorable prognosis and late recurrence. Thus, Ki-67 may reflect the aggressive behavior and predict the time of recurrence. It is therefore important to take the Ki-67 index into consideration in the follow-up of breast cancer patients.

P08-1

THE KOREAN HEREDITARY BREAST CANCER (KOHBRA) STUDY

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The Korean Hereditary Breast Cancer (KOHBRA) study is a prospective multicenter cohort study from 38 major centers identifying cases and their families. Between May 2007 and July 2011, the KOHBRA study enrolled up to 2,530 subjects and identified 501 mutation carriers. All participants received genetic counseling and BRCA genetic testing; clinical information and blood samples for blood banking were collected. The primary aim of the KOHBRA study I is to estimate the prevalence of BRCA1/2 mutations and ovarian cancer among a high-risk group of patients with hereditary breast cancer (BC) and their families. And the purpose of KOHBRA study II is as follows; first, to develop Korean BRCA mutation prediction model; second, to characterize clinical phenotype and discover novel prognostic factors for BRCA associated breast cancer; third, to identify environmental and genetic modifiers of BRCA1/2 mutation; fourth, to develop nationwide network of genetic counseling. The 1st part of KOHBRA study I is to estimate the prevalence of BRCA1/2 mutations among familial BC patients in Korea. We analyzed 775 familial BC patients who were enrolled in the KOHBRA study. Familial BC is defined as BC patients with a family history of BC or ovarian cancer (OC) in any relatives. Mean age at diagnosis of BC was 43.6 years old. The number of probands with family history of BC only and OC was 682 and 93, respectively. Overall prevalence of BRCA mutation among familial BC patients is 21.7% (BRCA1 9.3% and BRCA2 12.4%, respectively). Subgroup analysis showed the prevalence of BRCA mutation as follows; 19.6% among patients with BC family history only (BRCA1 7.6% and BRCA2 12.0%, respectively) and 36.6% among patients with OC family history (BRCA1 21.5% and BRCA2 15.1%, respectively). Most of the subgroup satisfied the 10% probability criteria to undergo BRCA testing. However, the prevalence of BRCA mutation among the subgroup, with two BC patients in a family with probands age at BC diagnosis older than 50 years old, was only 7.1%. We conclude that Korean familial BC patients are a good candidate for BRCA testing even with single- or 3rd degree relative-breast cancer family history. However, the probands age at diagnosis should be carefully considered when selecting a patient. The 2nd part of KOHBRA study I is to evaluate the prevalence of BRCA1 and BRCA2 mutations in non-familial breast cancer patients with high risk

factors in Korea. A subset of 758 patients was selected for this study from the KOHBRA cohort. Mutations in BRCA1 and BRCA2 genes were tested using F-CSGE, DHPLC or direct sequencing. Mutation of BRCA1/2 gene was identified in 65 (8.6%) patients (BRCA1 3.3%, BRCA2 5.3%). According to high risk groups, mutation of BRCA1/2 gene was identified in 53 (8.5%) of 625 early-onset breast cancer patients (age ≤ 40), in 22 (17.7%) of 124 patients with bilateral breast cancer, in 3 (50.0%) of 6 breast and ovarian cancer patients, in one (5.9%) of 17 male breast cancer patients, in 4 cases (6.1%) of 66 multiple organ cancer patients, and in 18 (22.8%) of 79 patients having two or more of these high risk factors. The prevalence of BRCA mutation in the subgroup of "age < 35" and "age ≥ 35" did not differ among patients with other risks (25.93% vs. 22.92%, $p = 0.78$). However, it was significantly different among patients without any other risk (9.96% vs. 2.87%, $p < 0.001$). We conclude that BRCA mutation for non-familial Korean breast cancer patients was detected at a high rate, particularly, in patients with an earlier onset (age < 35 without other risk or age ≤ 40 with other risk), bilateral breast cancer, breast and ovarian cancer, and two or more high risk factors. Genetic testing for non-familial breast cancer patients should be considered on an individual base. The KOHBRA study II began June 2010 and is being actively studied. The Western BRCA prediction models, Myriad II and BRCAPRO, were tested among Korean population and we found that these Western models underestimated the risk of BRCA mutation in Korean population and Korean BRCA mutation calculator is under development. When we analyzed the BRCA-related cancer in Korea, BRCA1-related breast cancer showed higher hormone receptor negative and triple negative breast cancers than sporadic breast cancer. BRCA2-related breast cancer showed similar characteristics as sporadic breast cancer. Genetic and environmental modifiers of BRCA mutation is under active investigation using GWAS study and epigenetic models. Korean Breast Cancer Society set up "genetic counseling academy" to train and certify nurses and other health-care professionals as a genetic counselor specialized for hereditary and breast and ovarian cancer patients. We are developing computerized interactive virtual counselor to overcome the lack of genetic counselor nationwide.

P08-2

HEREDITARY BREAST CANCER RISK ASSESSMENT AND THERAPEUTIC INTERVENTION IN MIDDLE INCOME ASIAN COUNTRY: EARLY EXPERIENCE FROM MALAYSIA

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Background: To date, more than 10 breast cancer predisposition genes have been identified, including high penetrance genes (e.g. BRCA1, BRCA2, TP53), moderate penetrance genes (e.g. PALB2, ATM, CHEK2) and common genetic variations (e.g. FGFR2, TOX2). In particular, the discovery of BRCA1 and BRCA2 in the mid 1990's has transformed the management of breast and ovarian cancer families and led to the development of a new class of therapeutic chemotherapeutic agents (PARP inhibitors). However, until recently, there have been fewer studies in Asian countries, in particular in middle and low income countries, because of the lack of resources (both manpower and funding) and lack of acceptability regarding genetic testing amongst both medical professionals and society.

Methods: From January 2003, all breast cancer patients treated at University Malaya Medical Centre were recruited to the Malaysian Breast Cancer Genetic Study. A blood sample was collected and germline DNA was analysed for mutations in BRCA1 and BRCA2 by full sequencing of intron-exon junctions and MLPA analysis; mutations in TP53 and PALB2 by full sequencing of intron-exon junctions; and for other genes by genotyping of selected mutations using the Sequenom MASSARRAY Genotyping platform.

Results: As part of the Malaysian Breast Cancer Genetic Study [MyBrCa], CARIF and University of Malaya have established a hospital-based cohort of breast cancer patients and to date, ~1,500 breast cancer patients have been recruited to the study. All patients who developed early onset breast cancer (< 35 years old) or had a strong family history of breast and/or ovarian cancer, were analysed for germline mutations in BRCA1 and BRCA2 by full sequencing and MLPA analysis. Of 400 index patients tested to date, approximately 60 index patients were found to have deleterious mutations in BRCA1 or BRCA2, and > 100 patients were found to have variants of uncertain clinical significance

(VUS). Further characterization of VUS were conducted using in vitro and population based studies. Genetic counseling and risk management in a specialized clinic were offered to all index patients and relatives with clinically relevant BRCA mutations and we studied the uptake and acceptance of screening and prophylactic surgery amongst BRCA carriers in our multi-ethnic and multi-religious population. In addition, all patients who developed breast cancer < 35 years old and were tested negative for BRCA mutations were tested for germline mutations in TP53. Of 86 patients who have been tested, 2 were found to have deleterious mutations, 3 with exonic variants that are likely to be clinically relevant, and a further 5 others had intronic variants. These results suggest that TP53 germline testing may be offered to a subset of breast cancer patients, particularly to those with early onset breast cancer and with Li-Fraumeni cancers in the family. In addition, all patients who had a moderate or strong family history of breast and ovarian cancer were tested for germline mutations in PALB2. Of the 150 patients tested to date, 1 deleterious mutation and 8 exonic variants have been identified. These results also suggest that PALB2 germline testing may be offered to a subset of breast cancer patients. For the remaining patients with no significant family history and/or late age of onset, we have developed a moderate cost genotyping approach to determine the prevalence of recurrent mutations in selected breast cancer predisposition genes.

Conclusion: In summary, we have found that the prevalence of germline mutations in BRCA1, BRCA2, TP53 and PALB2, are similar in Malaysia to that that has previously been reported in other populations, although the spectrum of mutations appear distinct. However, in part because of poor reporting of family history and lack of resources to support genetic testing, there remain challenges in risk assessment and therapeutic intervention in Malaysia.

P08-3

HEREDITARY BREAST AND OVARIAN CANCER: EXPERIENCE OF THE HONG KONG HEREDITARY BREAST CANCER FAMILY REGISTRY

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Background: Mutations in the BRCA1 and BRCA2 genes confer greater risk of developing breast cancer, ovarian cancer. Breast cancers due to underlying germline BRCA1/2 mutations are associated with particular pathological features that may differ from sporadic breast cancers. There is increasing knowledge that there may be ethnic differences in prevalence, types of BRCA mutations being carried and also breast cancer pathology types in different racial cohorts. The choice of management, once an individual has been found to carry the BRCA mutation, be it a choice of surveillance, prophylactic surgery or chemoprevention may differ in our locality compared to the West. Risk prediction models used have been developed based on Caucasian cohorts and this may have limited accuracy when used in the Asian population. Most publications to date are still mainly based on Caucasian cohorts although increasingly there are more Asian studies being published over recent years. Our study aims to present the local findings in Hong Kong, Southern China.

Methods: Data were obtained from a prospective database collected by the Hong Kong Hereditary Breast Cancer Family Registry since its establishment in 2007. High risk women based on their age and family history were recruited from both public and private hospitals and clinics of Hong Kong since March 2007. Medical information was prospectively collected from the patients and medical records. Epidemiological surveys, choice of management questionnaires were received from each individual. Data from our locality will be compared to Western published data and data from other Asian countries.

Results: From 1 March 2007 to 28 February 2011. 418 female probands has 33 male probands who had BRCA mutation screening performed using full gene-sequencing and Multiplex Ligation-dependent Probe Amplification (MLPA). 52 (12.4%) females and 7 (21.2%) males were found to be BRCA mutation carriers. For females, 53.8% were due to BRCA2 mutations whereas all male mutation carriers had BRCA2 mutation. A founder mutation c.3109C > T (p.Gln1037X), which was located in exon 11 of BRCA2

was confirmed. There were significant correlations between BRCA mutations and parity, having more family members with BRCA related cancers, age of diagnosis of breast and ovarian cancer, Triple negative breast cancers and cancers of higher grade. Majority of BRCA mutation carriers including those who are probands and family members who are found to carry the mutation agreed for intensive screening surveillance and 10-22% opted for prophylactic mastectomy (some being contralateral) and 21-33% for prophylactic salpingoopherectomy. Oral chemoprevention intake rate is 10-17%.

Conclusion: There are more BRCA2 mutations in Hong Kong Chinese cohort compared to the West. Choice of management differs with that reported in the West. The confirmation of a founder mutation allows founder screening prior to performing full gene-sequencing which improves the cost effectiveness in our locality.

P08-4

SINGAPORE

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STUDY AND MANAGEMENT OF HEREDITARY BREAST CANCER IN INDONESIA

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Incidence of breast cancer in Indonesia is 22 of 100,000 population, and is increasing at the moment, with high mortality rate since most of them found in the late stage. Breast cancer in Indonesia, as well as other Asian Countries, showed aggressive phenotype and tend to be younger ages compared with Western Countries. Breast cancer in Indonesia showed also lower estrogen receptor content. Regarding younger age of presentation of breast cancer, it might be assumed that hereditary portion should be higher than western counterpart. Previous study using Claus criteria in breast cancer patients in Yogyakarta and Jakarta from 173 hereditary susceptible breast cancer patients with DGGE showed 19 BRCA1, BRCA2 and BRCA1 and 2 mutations. Five BRCA1 mutations, 13 BRCA2 mutations and one double mutation (BRCA1 and 2) were found in this study. On going study is conducted for validation with High Resolution Melting technique to simplify the finding of mutations. Method of mutation analysis should also be chosen regarding cost-effectiveness in Indonesia. Risk assessment using Gail method and BRCAPRO also understudy, and family history seems to be very important. However, since there are some limitations in these methods, there must be another way to find high risk women to develop breast cancer in the future. Screening mammography could not be done for the population, and breast MRI for general population screening is more difficult to justify. Prevention methods of breast cancer also available such as chemoprevention, bilateral prophylactic mastectomy and bilateral salphyngo-oophorectomy, but promotion of healthy life style seems more acceptable due to cultural barrier. Indonesia, as developing country with limited resources should define the acceptable method for screening and prevention of breast cancer in high risk women, and collaboration in research and management with other Asian Countries is needed.

JAPAN

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Cross-sectional study of BRCA1 and BRCA2 mutations in Japanese patients suspected at least the same proportion compared with the study for non-Ashkenazi individuals in the US reported by Frank TS et al. (J Clin Oncol 2002; 20: 1480-90). Full sequencing analysis of BRCA1/2 gene showed 28 types of deleterious mutations in 36 subjects (26.7%), including 13 types of BRCA1 mutations in 17 subjects (12.6%) and 15 types of BRCA2 mutations in 19 subjects (14.1%), respectively. Risk factors for the presence of deleterious mutations of BRCA1/2 were indicated as follows: 1) families with breast cancer before age 40 within second degree relatives, 2) families with ovarian cancer and/or bilateral breast cancer within second degree relatives. Japanese investigator named Yoshio Miki (Professor of Molecular Genetics, Medical Research Institute, Tokyo Medical and Dental University at present) firstly reported BRCA1 gene as a strong candidate for the breast and ovarian cancer susceptibility (Science 266, 66-71 ,1994), however, the counseling and/or examination for BRCA1/2 has not routinely been done in Japan because they are not covered by health insurance. The cost of BRCA1/2 is more than 2,000 US dollars at present. Several exons were recognized which showed frequent mutation in particular of base sequences of BRCA1/2 among Japanese patients and the screening test called N-set for HBOC high-risk individuals with selected exons which showed frequent mutations characteristically in Japanese patients in addition to exons that have already been reported by other Japanese researchers as frequent mutation has been available. The current governmental reinsurance system does not cover any genetic testing for risk assessment of future onset of diseases. So, cost bearing from her (his) own pocket often makes it difficult for getting test. N-set costs patients lower in price than that of conventional entire sequence analysis. This may increase an opportunity to undergo the screening test to patients suspected to have HBOC and their blood relatives. They are able to know their own risk of developing cancer to be higher or average through the test result. It is expected that once patients know their own risk of cancer are anxious to prevent the future onset of these diseases and undergo frequent health checkups; thereby they could obtain an opportunity for earlier detection. Japan Breast Cancer Society (JBCS) has strongly requested that this test should be covered by governmental reinsurance in the near future. And JBCS has conducted the research project related to this topic. The project consists of 5 items. 1) To investigate the current status of counseling system and

strategies for HBOC in other countries. 2) To investigate the same issues in our country. 3) To develop a homepage for patients and medical professionals to access the proper information related to HBOC. 4) To create a national database related to HBOC. 5) To make the clinical guideline including counseling and strategies (screening, diagnosis& treatment and prophylaxis).

P08-7

BRCA1/2 GENE MUTATION IN CHINESE BREAST CANCER PATIENTS

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Recent trends indicate that incidence of breast cancer is rising in China, especially in large city, such as Shanghai. About 10-15% breast cancer patients were hereditary one, and the most important genes were BRCA1 and BRCA2. So far, only a few of studies have been performed in this field in China mainland. In the past 8 years, we performed the BRCA1/2 mutation detection in 489 cases of Chinese high-risk breast cancer patients, and found 44 cases of mutation carriers (23 cases in BRCA1 and 21 cases in BRCA2). Comparing to the BRCA1/2 mutation carriers in Caucasian, We found some different characteristics in Chinese one. Two recurrent mutations in BRCA1, 1100delAT and 5589del8, were identified. The recurrent mutations account for 34.8% BRCA1 mutations in our series. In the historical reports, BRCA1 1100delAT was found in both Asian and Caucasian, while BRCA1 5589del8 was only found in Chinese and Korean population. Interestingly, as the family history of ovarian cancer (26.7% vs. 11.9%) doubled the incidence of BRCA1/2, the family history of gastric cancer played the similar role in Chinese breast cancer population (23.8% vs. 11.8%). In our study, the incidence of BRCA1/2 mutation in the selected high-risk breast cancer patients was only 10-15%. In order to increase the efficacy of mutation detection, we tried to use some predictive model to perform the pre-detection assessment, but most of the predictive models were build in the data of Caucasian, they could not be used well in Chinese population because of the ethnic differences between these two populations. Using the specific characteristics in Chinese BRCA1/2 mutation carriers, a model was built to predict the possibility of BRCA1/2 mutations in Chinese population. The higher accuracy was achieved by the predictive model when compared to the BRCApro models, presenting the higher sensitivity, PPV, NPV and area under ROC curve.

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BREAST CANCER SCREENING IN KOREA

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Breast cancer is the most common cancer as well as the leading cause of cancer death in women worldwide. In Korea, breast cancer is one of the most prevalent cancers from 2001. According to reports of the Korea Central Cancer Registry, the incidence of the breast cancer has been increasing rapidly. The incidence was 14.7% in 2008. The cause of the increase in breast cancer incidence in the Korea may be explained in large part by increased use of screening mammography, which detects small non-palpable tumors. Other possible causes are prolonged exposure to estrogen from westernization of lifestyle; early menarche, delayed menopause, changes in patterns of childbearing with a trend toward delayed first birth and decreased parity, increasing use of hormone replacement therapy. The characteristics of Korean Breast Cancer are as follows: Increase in the number of patients and the incidence rate; Increase in the ratio of patients whose breast cancer was detected through screening mammography; Increase in the rate of DCIS and early cancer; High proportion of young age premenopausal patients; Good prognosis in most stages.

In Korea, national cancer screening program (NCSP) began in 1999 for five major cancers, including stomach, breast, uterine cervix, liver and colorectal cancers. The protocol of the NCSP was constructed around evidence-based literature and the current national screening policy by the Support & Evaluation Board of the NCSP in the National Cancer Center as well as associated academic societies. The NCSP recommends biennial breast cancer screening for females over 40 years of age with mammogram ± clinical breast examination as the screening tool.

The Korean Society of Breast Imaging (KSBI) developed guidelines and standards of quality management for mammography from 1999. On January 14, 2003, the national assembly of Korea approved the Acts including quality management for mammography. Annual inspection includes the facilities to meet minimum quality standards for personnel, equipment, and phantom image. Every three year, on site survey and evaluation of clinical image are added. Mammography accreditation program has been helping facilities improve the image quality by peer review and professional feedback.

The breast cancer screening rate increased from 33.2% in 2004 to 55.2% in 2009. According to previously published reports in Korea, there were variations in performance indicators across the institutions, but these differences were not extreme; Performance of

screening mammography was associated with sensitivity of 85.0-91.5%, specificity of 95.0-99.0%, PPV1 of 0.8-2.5%, PPV2 of 18.0-27.7%, recall rates of 5.1-13.0%, and cancer detection rates of 0.5-2.0/1,000. Compared with the ideal goal of ACR in USA, PPV1 and cancer detection rates are lower than the goal of ACR. It is probably due to lower cancer incidence in Korea than that of USA. In the near future, results of 10 year performance and outcome measurements of NCSP in Korea will be reported.

Although mammography screening is the only method presently considered appropriate for mass screening of asymptomatic women, the success in cancer detection has been limited in women with small and dense breasts, especially in Asian women. Other or new breast imaging technologies having potential role in breast screening are digital mammography, breast ultrasound including automated whole breast US, MRI, digital breast tomosynthesis. The digital mammographic imaging screening trial (DMIST) found that digital mammography performed significantly better than analog mammography in premenopausal and perimenopausal women, those aged < 50 years, and those with dense breasts. Ultrasound is an ideal supplement to mammography. The results of a multicenter trial of supplemental screening breast ultrasound for women at high risk with dense breast tissue have been promising. Several studies found that ultrasound alone caught breast tumors that mammography couldn't see in 0.1-0.5% of patients. Previously Published Data of screening US in Korea show similar cancer detection rate, reported 0.35-0.5%. However, the operator dependence of handheld ultrasound is a major concern with respect to the widespread use of whole breast screening ultrasound. Recently developed automated whole breast ultrasound is more readily reproducible, has 3D capability through multi-planar reconstruction, and allows delayed interpretation outside of real time, optimizing the radiologist's reading environment. Magnetic resonance imaging has been used with success in the screening of high-risk women. From 2007, the ACS issued recommendations for screening breast MRI among certain high-risk women. Recently developed digital breast tomosynthesis (DBT) allows cross-sectional visualization of breast tissue that the overlying and underlying anatomical tissue can be effectively removed when viewing individual slices. Thus overcoming the problem of super-positioning that reduces the effectiveness of mammography. It also has a potential role for breast screening. However, there are no large, peer-reviewed studies that support the routine use of other imaging techniques, these are not recommended to be widely used until a clear outcome benefit is established for breast cancer screening.

BREAST CANCER SCREENING IN JAPAN

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Breast cancer is now the most common cancer among females in Japan and the number is steadily increasing. A serious issue is that the number of breast cancer deaths is continuously increasing, too. Early detection of breast cancer by a modality proven to be effective by randomized controlled trials (RCT) provides the potential to reduce breast cancer deaths. It is now in widespread agreement that screening mammography (MMG) is the only useful modality for early detection of breast cancer. In Japan, mammographic screening for breast cancer started in 2000 for women over 50 years of age. This was expanded to women aged 40 and over in 2004. The method of screening consists of biennial MMG combined with inspection and palpation. But the checkup rate of mammographic screening is very low, approximately 20%, compared with more than 60% in Europe and the U.S.A. Therefore, the Japanese government introduced a new project in 2009 in which a free coupon for mammographic screening is issued every five years for women between 40 and 60 years old. The checkup rate increased slightly after the introduction of free coupons, but it has not yet reached 50%. There are some reasons for the low checkup rate: 1) Little interest in breast cancer or having no problem about the breast (misunderstanding of the purpose of screening); 2) No time or opportunity, and inconvenient location of institute for mammographic screening; 3) Cost for mammographic screening; etc. It will take really hard work to achieve our goal of the 50% checkup rate. On the other hand, mammographic screening alone is not effective to detect early breast cancer in dense breasts. Dense breasts are common at ages below 50 in Japanese women. Ultrasonography (US) has the potential to detect early breast cancers not found by MMG, and several single institutional studies have already started using supplemental ultrasonic screening for breast cancer in Japan. But, worldwide, RCT have not been completed to assess the efficacy of ultrasonic screening to reduce breast cancer mortality. Therefore, in 2006 the Japan Strategic Anti-cancer Randomized Trial (J-START) started to verify the effectiveness of ultrasonic screening for breast cancer for women aged 40-49 years. This trial was designed for 50,000 women with MMG and US (Study group), and 50,000 women with MMG only (Control group).The primary endpoints of this trial are the comparisons of sensitivity and specificity, and the secondary endpoint is a comparison of the accumulated incidence rate of advanced breast cancer. This is a multi-institutional prospective RCT, and more than 75,000 women from 42 institutions have

participated as of March 31, 2011. Two years after the first recruitment, the participants will be recalled to be screened for a check of their health status, incidence of breast cancer, history of hospital visit with any breast symptoms, and so on. It will take a long time until the effectiveness of ultrasonic screening combined with MMG for women aged 40-49 years can be proven. Therefore, we have to promote mammographic screening further for the achievement of a 50% checkup rate nationwide.

BREAST CANCER PREVENTION

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Currently there are two endocrine agents that are U.S. FDA approved for breast cancer prevention. Tamoxifen and raloxifene are selective estrogen receptor modulators and have been shown to reduce the risk of invasive and non-invasive breast cancer by 40-50% in high risk women. Although these agents are in the same drug class there are important differences between them particularly in regard to side effects, notably raloxifene is not associated with an increased risk of endometrial cancer or cataracts. Both agents are associated with an increased risk of thromboembolic events, but the risk is lower on raloxifene compared with tamoxifen. New data also shows that exemestane, a steroidal aromatase inhibitor, has efficacy in reducing risk of breast cancer. In the MAP.3 trial postmenopausal women at increased risk for breast cancer on exemestane decreased risk by 65% compared with those on placebo. The incidence of bone fractures and cardiovascular events did not differ between the intervention and placebo arms. Currently there is no data comparing tamoxifen or raloxifene head to head with an aromatase inhibitor, however trials are ongoing. At this time it is clear that there are a number of effective agents and that selection of a particular agent should be made in the context of the overall health and concerns of the patient. Of note only tamoxifen has been proven effective in premenopausal women. Raloxifene and exemestane can only be used in postmenopausal women. Unfortunately few women are using these agents for prevention.
We now have three agents that are directed at preventing hormone receptor positive breast cancers, and none for hormone receptor negative breast cancer. This underscores the importance of understanding breast carcinogenesis and evaluating potential biomarkers of activity before moving agents into large costly phase III trials. One biomarker of interest is mammographic density (MD). Increased MD is an independent risk factor for breast cancer with approximately 4-fold increase in risk observed comparing those women with most dense tissue to least dense tissue on mammogram. Endocrine therapies are known to modulate MD and a recent publication (Cuzick et al. JNCI 2011) shows that tamoxifen induced change in MD can serve as a surrogate marker of risk reduction. Evaluation of at risk breast tissue is also feasible in the prevention setting and there are a number of ways tissue can be sampled and evaluated; techniques include breast core biopsies and random peri-areolar fine needle aspiration (RPFNA). Each technique obtains breast epithelial cells so that changes in breast tissue can be evaluated in

response to an intervention. Recent data shows that RPFNA can be instituted across multi-institution studies with high degrees of reproducibility. Cells are often evaluated for change in atypia but markers of proliferation and molecular targets can also be assessed. In currently accruing phase II breast cancer prevention trials these intermediate biomarkers typically serve as study endpoints. Current challenges in breast cancer prevention include validating biomarker endpoints, identifying agents that have activity against ER negative breast cancer, increasing the use of active agents in at risk patients, and identifying the active dose and duration of agents.

DETERMINING FACTORS OF BREAST CANCER SURVIVAL IN SEOUL BREAST CANCER STUDY

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A number of studies suggested the association between breast cancer survival and lifestyle factors including obesity, physical activity, diet, and reproductive factors. However, these finding are inconsistent across ethnicities and study designs. To investigate the determining factors of breast cancer prognosis and survival, 3,047 incident breast cancer women were recruited. During follow-up with a median of 4.2 years, 389 recurrence and deaths occurred. At recruitment, questionnaire data were collected on demographic, lifestyle, reproductive, and dietary factors at breast cancer diagnosis. Patients who did regular exercise before diagnosis showed better disease free survival. The hazard ratio estimates were 0.6 (95% CI = 0.4-0.9, $P = 0.02$). In the study of genome-wide association study using Affymetrix SNP Array 6.0 Chip, several genetic variations were associated with breast cancer recurrence and death after adjusting known clinicopathological factors. DNA methylation profile was investigated between ER/ PR status using Infinium Methylation Assay. In the two-stage study, DNA methlyation status of *FAM124B* ($P = 7.26 \times 10^{-7}$), *ST6GALNAC1* ($P = 2.85 \times 10^{-6}$), *NAV1* ($P = 5.94 \times 10^{-6}$) and *PER1* ($P = 6.45 \times 10^{-6}$) were associated with ER and PR status. The elevated serum levels of lipocalin and MMP-9 were associated with poor breast cancer prognosis. Patients with high levels of both proteins exhibited 1.9-fold hazard for disease free survival compared to patients with low levels of both proteins (95% CI = 1.2-3.0, $P_{trend} = 0.012$). A comprehensive and systematic approach will be implemented to better identify the determining factors of breast cancer survival in the future.

SP03-1

INDIVIDUALIZATION FOR THERAPEUTIC MANAGEMENT OF LUMINAL SUBTYPE BREAST CANCER

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Personalized medicine for breast cancer is becoming very important as seen with new molecular diagnostic tools such as Oncotype DX and Mammaprint. Luminal subtype breast cancer account for predominate population in Asian breast cancer. They are treated with hormonal therapy. The prediction of hormonal therapy is still conducted with classical molecular biomarkers such as ER and PgR, but their accuracy is insufficient to categorize the eligibility of hormonal therapy. Recently diagnostic performance of Ki67 is being discussed with respect to additional chemotherapy to luminal subtype breast cancer in adjuvant setting. The ambiguity of the efficacy of the therapy to luminal subtype could be derived from the different intracellular estrogen signaling property in individual's cancer. Hormone refractoriness might also be related to these different properties of ER signaling. We are investigating the mechanisms of these different responses to hormonal therapies and chemotherapies relevant to estrogen signaling pathways in breast cancer by estimating transcription activity of ER in cell isolates. We constructed adenovirus reporter vector that had Green Fluorescence Protein (GFP)-cDNA connecting Estrogen Response Element (ERE) in the 5'-upstream of the gene, and infected into isolated cells from surgical specimens. The ER activity in individuals was estimated by the GFP expression under fluorescent microscope. We found discrepancy between expression of current prognostic factors and ER transcription activity among individual's cells isolated from 62 primary breast cancers using this adenovirus ERE-GFP assay system. The activity of ER is seemed to have distinct significance from ER protein expression in breast cancer, indicating ER expression might be not perfect predictive factor for hormonal therapy. Furthermore, ER activity was affected the efficacy of chemotherapy such as taxan. We found that ER diminished the efficacy of taxan to ER-positive breast cancer via ER-target gene. Moreover, cell isolates from 10 aromatase inhibitor-refractory cancer specimens showed diverse ER activity and varied sensitivity to anti-estrogens by the adenovirus ERE-GFP assay. Previously, we stably transfected ERE-GFP reporter DNA in ERalpha-positive breast cancer cells (MCF-7), and established a reporter cell

line (named E10) which can analyze ER-activating ability in the living cells. Then we carried out in vitro studies using several cell lines established from the MCF-7-E10 cells, which mimic the aromatase inhibitor resistant cancer. The results revealed the existence of multiple and alternative ER activating signaling pathways such as protein phosphorylation-dependent or androgen metabolite-dependent manners in the hormonal therapy-resistant breast cancer cells. All of these results indicate that the individualization of luminal subtype breast cancer is very important for decision of therapeutic management in not only hormonal therapy but also chemotherapy or molecular target therapy. To accomplish this individualization, novel accurate biomarkers, which reflect the intracellular estrogen signaling, must be required. In this aspect, further basic study for the molecular mechanisms of variety and alteration of estrogen signaling pathway will be needed.

SP03-2

PATHOLOGIC AND CLINICAL ASPECTS OF LUMINAL SUBTYPE BREAST CANCER

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Breast cancer is a disease showing heterogeneity in molecular, pathologic and clinical aspects. Since the advent of microarray analysis, a number of studies have led to the identification of five molecular subtypes associated with differences in survival and different clinicopathlogic parameters: luminal A, B and C, Her-2 positive and basal-like subtypes. Luminal C is normal breast like group. Luminal A and B subtypes express characteristic of luminal cell lineage. Of note, ER status alone can reliably distinguish between broad groups of these subtypes as most of luminal A and B tumors are ER positive and the majority of Her-2 positive, basal like and normal like tumors are ER negative. Within the group of luminal epithelial subtypes, the largest group, luminal A tumors are characterized by a higher level of expression of luminal specific genes (e.g., ER, GATA3, LIV-1, HNF3A, XBP1) and lower level of expression of proliferative genes (e.g., cyclinB and Ki-67) as compared to the second, smaller group, luminal B tumors (low expression the ER cluster and high expression of a novel set of beges such as CCH, LAPTMB4, NSEP1 and CCNE1). In practically, subgroups can be classified by immunohistochemical surrogates as luminal A (ER and/or PR positive and Her-2 negative) and luminal B (ER and/or PR positive and Her-2 positive). Existing data from gene expression base studies and from studies using simplified IHC based definition, luminal A tumors are low grade and associated with an early stage at the diagnosis and have favorable prognosis. Patients with luminal B tumors appear to experience a slightly, but not significantly poorer prognosis than patients with luminal A tumors, but patients with tumor of either luminal subtypes may be expected to benefit from hormonal therapy. Although the basal-like and Her-2 subtypes are repeatedly recognized in independent data set, discernment of the ER-positive subtypes has been problematic. Perou et al. described a proliferation cluster of genes that correlated with cellular proliferation rates and was noted to have considerable variation between subgroups. Taking this concept further, Loi et al. reported high or low-genomic grade subgroups of luminal tumor using genomic grade index (GGI) which are highly comparable to the preciously described luminal A and B subclassification and significantly correlated to the risk groups produced using the 21 gene recurrence score. Meanwhile, in ER+ Her-2- disease, the proliferation index clearly divides the popula-

tion into two different disease. There are the highly proliferative luminal B and the low proliferative luminal A tumors. To detect the status of proliferation activity, a tumor maker such as Ki-67 has been used as potential tool. However, it is challenged by a lack of interobserval consistency and quality control of immunohistochemical staining. In addition, there are no clear criteria of the optimal cutoff between them. Another suboptimal tool is tumor grade. Although it can be used, there is still a challenge in classifying grade 2 and interobserval consistency especially in grade 1. Gene expression signature and GGI could resolve some issues of them. In an era of personal treatment, there will be better tools to distinguish between them. Current studies suggest that luminal A and luminal B tumors are completely different diseases and study is being performed to better discrimination between tow subgroups of luminal tumors and apply effective treatment to each patients including endocrine and chemotherapy.

SP03-3

ESTROGEN RECEPTOR STATUS PREDICTION BY GENE COMPONENT REGRESSION: A COMPARATIVE STUDY

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Background/purpose: The aim of the study is to evaluate gene component analysis for breast cancer estrogen receptor (ER) status prediction. Modern microarray techniques have inherited the n (experimental samples) $< p$ (gene expression features) problem and one method to tackle this problem is to reduce the high dimensional gene expression features and use synthesized latent factors (gene components) instead. The impact of gene selection, gene component regression and predictive methods were evaluated through two publicly available breast cancer microarray datasets, and the proposed classifiers was tested in our independent microarray experiments of Taiwanese breast cancers.

Methods: Three dimensional reduction strategies, principle component regression (PCR), partial least square (PLS) and reduced rank regression (RRR) were applied to publicly available breast cancer microarray dataset and the derived gene components were used for tumor classification by logistic regression (LR) and linear discriminative analysis (LDA). Three gene selection criteria including phenotype correlation, coefficient of variance and two-sample t-test were evaluated as well. The classification/predictive performance of gene component regressions were further compared with that of support vector machine (SVM) and K-nearest neighbor (KNN), both of which based on individual genes rather than gene components.

Results: From training data we learned that PCR might perform virtually as well as PLS when genes were carefully selected, i.e. genes were chosen from their ER correlations and the maximal covariance between explanatory and response variables of PLS seemed superfluous. However, when genes were selected from their variability (coefficient of variance), the accuracy of PCR declined rapidly compared with PLS and PCR-LDA was compromised more than any other gene component algorithm. Through our experiments, PCR occasionally demanded more than one gene component to deliver the most optimistic regression model, indicating a more sophisticated role of PLS for tumor classification under circumstances where gene selection was not outcome-oriented (unsu-

pervised gene selection). When derived classifiers were projected into our 44 breast cancer samples, an immediate deterioration of prediction error about 10% was noted (Fig. 1) and the slight superiority of PLS over PCR in training data diminished, meaning that supervised gene component classification was not always better or equal to unsupervised PCR, as evidenced by the preferable PCR-LDA combinations in our experiment with the top 79 differentially expressed genes. Our study also showed benchmark comparison of 1-NN, 3-NN and SVM. Both PCR and PLS were equivalent or superior to SVM and K-NN in two training datasets, but when validated in independent data, SVM ranked as the worst with the highest misclassifications while PLS shared comparable prediction accuracy with K-NN. Stepwise logistic regression and discriminative analysis were used to identify important genes constituting gene components from different combinations of feature selection and prediction model and these candidate genes included *ESR1, C4A/C4B, TPBG, SLC39A6, NDP, AGTR1, CRISP3, CMYA5, EN1, AGR3, CDC20, DCD, PCSK1* and *DLK1*.

Conclusion: We demonstrated that gene component classifiers could reduce the high-dimensionality of gene expression data and the collinearity problem inherited in most modern microarray experiments. In our study gene component analysis could discriminate ER positive breast cancers from negative cancers and the proposed classifiers were successfully reproduced and projected into independent microarray dataset with high predictive accuracy. Keywords: gene component, dimension reduction, principle component regression, partial least square, microarray, breast cancer, estrogen receptor.

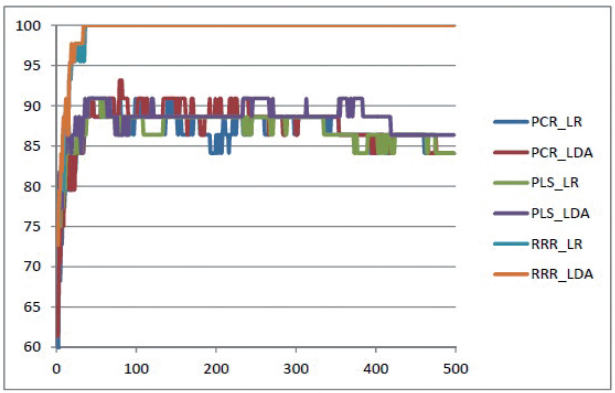

Fig. 1 Prediction results using the differentially expressed genes as entry variables. (Horizontal axis: enrolled gene numbers, vertical axis: percentage of accuracy)

SP04-1

PREOPERATIVE AXILLARY STAGING

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Axillary Lymph Node (ALN) status is one of the most important prognostic indicators in breast cancer. The status of ALN might influence on the decision and the choice of adjuvant systemic therapy. Accurate evaluation of ALN involvement is mandatory before treatment of primary breast cancer since the introduction of sentinel node biopsy (SNB). Complete extirpation of ALN cannot eliminate the micrometastatic cancer cells and it is frequently associated with debilitating arm edema. Nowadays, axillary lymph node dissection is regarded as a staging procedure rather than curative one. However, we have to keep in mind that certain proportion of breast cancer patients with extensive ALN envovement can be cured by curative ALN removal and enjoy long-term disease free status. Wide acceptance of neoadjuvant chemotherapy even in early stage breast cancer urges accurate axillary staging before surgery in recent years. Most frequently used methods for preoperative axillary staging are ultrasonography (USG), CT, MRI, and PET-CT. Each method has an advantage and disadvantage over one another in terms of sensitivity and specificity. Meta-analysis of each method indicates that all imaging modalities have comparable accuracy in preoperative axillary staging. USG is convenient and practical method whereas the procedure is vulnerable to expertise of clinician or radiologist. In contrast, PET-CT and MRI can provide more objective image albeit both frequently show higher false-positive result compared with USG. Preoperative axillary evaluation can be more accurate by multimodal manners such as USG, CT, MRI, and PET-CT. In terms of cost-benefit effect, USG-assisted ALN cytology seems to be a reasonable method for preoperative axillary staging in early breast cancer, although the procedure is depend on expertise of clinician. For the patient planning neoadjuvant systemic therapy, pretreatment sentinel node biopsy is more accurate method compared to post-treatment SNB.

RECENT ADVANCE AND CONTROVERSIAL ISSUS IN SENTINEL NODE BIOPSY

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For a long period of time, axillary lymph node dissection (ALND) and histopathologic evaluation of the axilla has represented the gold standard for determining the status of the regional lymph nodes, the
prognosis, and the appropriate treatment of patients with breast cancer. But in patient with early breast cancer, particularly in the clinical stage I, the axillary nodes fail to contain metastases in over 75% of cases. Sentinel lymph node biopsy (SLNB) with less surgical morbidity and the same accuracy in determining the prognosis and treatment of patients has emerged as a feasible alternative to ALND. SLNB is rapidly becoming the standard of care for a patient with early breast cancer. Axillary lymph node dissection (ALND) is considered unnecessary when sentinel lymph nodes (SLNs) are negative. The main goal of SLNB is avoiding the unnecessary removal of uninvolved lymph nodes and preventing the morbidity of a standard ALND. Recent randomized clinical trials have already proved less surgical morbidity and better QOL for SLNB alone compared with ALND. However, there are several controversies about SLNB remain:

1) What are the indications of SLNB?
2). Should a complete axillary dissection be performed when the SLNB is positive?
3) Can lymphedema occur after SLNB?
4) What is the accuracy of SLNB in patients who have received neoadjuvant therapy prior to surgery?
5) Technical considerations about SLNB

1) The indications of SLNB:

Since 2005, the NCCN guidelines made the recommendation for use of SLNB in single or multicentric T1 and T2 tumors, but not in T3,T4 or inflammatory cancers. Previous axillary and breast surgery, neoadjuvant systemic and obvious palpable axillary nodes are considered relative contraindications. The older age, obesity, and male breast cancer are acceptable, but not recommended in pregnancy women due to lack of safety data. The evaluation of internal mammary nodes(IMNs) by SLNB is acceptable, although the discovery of positive IMNs is considered only beneficial to those who are axillary

node negative.

2) Should a complete axillary dissection be performed when the SLNB is positive?

The current paradigm for nodal spread is that metastasis occurs sequentially from the primary tumors to the SLN and then to non-SLNs; thus completion ALND can be avoided in SLN-negative tumors. If the SLN is positive for metastatic disease, the standard management is completion ALND. However, only 50 per cent of patients with metastatic disease in the SLN have further non-SLN involvement. So it has been suggested that completion ALND may be not necessary in women with SLN metastasis but low risk of non-SLN involvement. Isolated tumor cells (ITC), and micrometastasis (0.2-2 mm) in SLN may be reasonable for omitting ALND. Recently data from Z0011 trials suggested that even SLN metastasis, those who underwent BCS and SLNB only still have low regional recurrent rate. The data suggested radiotherapy plays some important role in local regional control. Completion ALND may be omitted in case of adjuvant radiation was delivered to the axilla.

3) Can lymphedema occur after SLNB?

Lymphedema represents one of the major factors contributing to postoperative morbidity as it may result in decreased range of motion, pain, weakness, or stiffness of the affected extremity. The incidence of lymphedema after level I and II ALND has been reported in the literature between 5% and 25%. The extent of axillary surgery and postoperative axillary irradiation are the 2 most common factors contributing lymphedema. In Z0011 the surgical complications associated with SLNB plus ALND group was much higher as compared with SLNB only group (75% vs 25%). Rates of lymphedema with SLN were much lower in the same study (13% vs 2%).

4) What is the accuracy of SLNB in patients who have received neoadjuvant chemotherapy (NAC) prior to surgery?

Neoadjuvant chemotherapy is still considered as a contraindications of SLN biopsy. It has been suggested that chemotherapy may interfere with anatomy and physiology of the lympatics and may therefore have adverse effects on the accuracy of SLN procedure. In a meta-analysis of SLN biopsy, the false negative rate of NAC group about 1.5-3 times higher than Non-NAC group. The accuracy of SLNB is controversial in these trials. There were still insufficient data to recommend SLN for patients receiving NAC.

5) Technical considerations about SLNB

Factors affect the identification of the sentinel node are lymphoscintigraphic imaging, Gamma probe, mark on the skin, type of radiocolloid, injection site, obese and elderly, imaging time and doses of tracer. Lymphoscintigraphy is not a substitute for probe-based surgery but is adjunctive. Lymphoscintigraphy is helpful for identifying whether the radiocolloid has drained to the axilla or to other possible sites of drainage. Using larger colloids are preferable. Peritumoral and periareolar injection was preferred. Obese and elderly patients tend to have a higher frequency of false negative rate. Imaging done soon after injection of radiocolloid is not recommended. Imaging done 6 to 18 hours after injection is considered better. Typically at least 10mBq 99mTc colloid is considered adequate dose.

SP04-3

PREDICTORS OF LYMPH NODE METASTASE IN BREAST CANCER

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Axillary Lymph Node (ALN) status is the most accurate predictor of clinical outcome in breast cancer. Decisions on adjuvant chemotherapy and postmastectomy radiotherapy depends on not only axillary nodal status, but the number of nodes involved with tumour. Clinical evaluation of the axilla has been shown to be unreliable. Hence a form of axillary dissection is required to obtain axillary nodal status. However axillary dissection has been shown to be associated with complications such as pain, lymphoedema and shoulder stiffness. Sentinel node biopsy reduces the incidence of such complications and is not associated with an increased risk of regional recurrence. However, this procedure is expensive and may not be feasible in low and middle income countries where resources are limited and women present with large cancers. Predictors of axillary node metastases have been studied. In T1 tumors, the reported incidence of lymph node metastases ranges from 21% to 35%. Primary tumor characteristics can be used to identify a subgroup of patients with a low risk of ALN metastases in T1 breast cancer, such as grade, size, lymphovascular invasion and a low Ki-67 staining, and preoperative risk assessment might be used to omit routine ALN dissection in those patients at low risk of ALN metastases A retrospective study of 953 women with T1 and T2 invasive breast carcinoma and axillary dissection in the University Malaya Medical Center between January 2001 and December 2005, showed that 7.7% of T1a tumours, 12.3% of T1b tumours, 29.2% of T1c tumours and 48.2% of T2 tumours had node involvement. Out of the 769 patients (80.7%) who had presence or absence of lymphovascular invasion (LVI) reported in the pathology report, 24.4% of patients where there was no LVI had axillary node metastases compared with 52.2% of patients where LVI was reported. On univariate analysis, diameter of tumour > 2 cm, presence of lymphovascular invasion, and higher grade (2 & 3) tumours were significantly associated with a higher risk of nodal metastases. However on multivariate analysis, only lymphovascular invasion and tumour size were independent predictors based on the logistic regression. In T1 tumours, ALN dissection will overtreat almost 75% of cases; hence a sentinel lymph node biopsy is justified in these tumours. In T2 tumours, where almost 45% have lymph node involvement, sentinel node biopsy may not be cost-effective. In centres where women more often pres-

ent with T1 tumours, sentinel lymph node biopsy would be a cost-effective approach, and should be introduced as an option for women with clinically node negative T1 breast cancers. Once a sentinel lymph node programme is established, it can be extended to include clinically node negative T2 tumours, where it may not be as cost-effective since the incidence of node positivity is higher, but will avoid a formal axillary dissection in those women who are node-negative. Hence predictors of lymph node metastases, particularly size and lymphovascular invasion could be used to identify a subset of women who may benefit from minimal axillary surgery.

SP05-1

HER2 POSITIVE BREAST CANCER: TRASTUZUMAB AND CURRENT TREATMENT STRATEGIES

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Breast cancer is known to be heterogeneous disease, characterized by largely 3 subtypes. The current treatment for breast cancer includes chemotherapy, endocrine therapy and biological therapy. Treatment has become more subtype-oriented based on characteristics of the tumor including positivity of the human epidermal growth factor receptor (HER)-2. About 20-25% of early breast cancer patients have HER2 positive tumors. HER2 positivity was a negative prognostic factor for survival in the past; however, with the advent of anti-HER2 therapy, trastuzumab, prognosis has become similar to or superior to HER2 negative disease. Clinical benefit from trastuzumab-based therapy in both early and advanced BC has been demonstrated. With the administration of trastuzumab for one year in the adjuvant setting, disease recurrence decreased by 50% and mortality by 30%. However, controversy exists in the use of trastuzumab, including the sequence of adjuvant trastuzumab (concurrent with chemotherapy or sequential) or the treatment duration (< 1 year, 1 year or 2 years), or the indication for very small size breast cancer, or the best combination chemotherapeutic drugs, or the treatment choice upon disease progression in metastatic setting. Lapatinib, an oral tyrosine dual kinase inhibitor, which blocks both the epidermal growth factor receptor and HER2 receptor has been approved by the FDA, and lapatinib in combination with capecitabine has become the standard of care after the first line trastuzumab failure in Korea. The benefit of trastuzumab use beyond progression has also been shown, which indicates the need for continuous suppression of the HER2 pathway. Targeting both HER2 and other pathways may enhance the clinical benefit observed with trastuzumab and overcome potential resistance. Current trials are ongoing to help answer these questions. Other novel anti-HER2 drugs including pertuzumab, trastuzumab-DM1 (T-DM1), or Neratinib have entered phase II and III clinical trials.

HER2-DIRECTED THERAPY/DEVELOPMENT OF T-DM1

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SP05-3

HER2 PATHWAY BIOLOGY FOCUSING ON P95

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HER2 (also known as ErbB2, neu), is a tyrosine kinase that belongs to the epidermal growth factor receptor (EGFR) family. Underscoring its unique value as a biomarker, one type of breast cancer is named after HER2. HER2-positive cancers account for 20-30% of total breast cancers, they are characterized by overexpression of the receptor because of gene amplification. In addition to a reliable biomarker, HER2 is a validated therapeutic target. Trastuzumab, a monoclonal antibody against the extracellular domain of HER2, has contributed to the increase in survival rates of breast cancer patients observed during the last decades. However, this success has been limited because a substantial proportion (~70%) of HER2 positive breast cancers are either intrinsically resistant to the treatment with trastuzumab or develop resistance after treatment. Lapatinib, a tyrosine kinase inhibitor that targets HER2, has been recently developed as an alternative treatment for HER2 positive cancers (1). This presentation will focus on recent developments in the understanding of a series of HER2 fragments, collectively known as p95HER2 or HER2 CTFs (Carboxy Terminal Fragments), that may constitute a novel biomaker for an aggressive subtype of HER2-positive cancers with distinct biological and clinical features. p95HER2 fragments arise through, at least, two different mechanisms: proteolyic shedding of the extracellular domain of the full-length receptor (2) and translation of the mRNA encoding HER2 from internal initiation codons (3). The shedding of the ectodomain of HER2 is likely carried out by the metalloprotease ADAM10 and occurs at a site proximal to the transmembrane domain, generating a 95-100 kDa p95HER2 fragment (4, 5). As a result of the alternative initiation of translation two p95HER2 fragments of 100-115 kDa and 90-95 kDa, also known as 611-CTF and 648-CTF, respectively, are generated. These p95HER2 fragments are active, although they differed in their potency. While the activity of the 95-100 kDa (648-CTF) fragment was comparable to that of the full-length receptor, expression of the 100-115 kDa (611-CTF) fragment led to a much more rapid and acute activation of the different signaling cascades activated by HER2 (6) Sperinde et al and Parra-Palau et al generated monoclonal antibodies that specifically recognize 100-115 kDa p95HER2. The classification of breast cancer patients according to the levels of expression of 100-115 kDa p95HER2, judged by immunohistochemistry with the specific antibodies confirms that, indeed, the tumors positive for this HER2 fragment constitute a sub-

group of HER2-positive breast cancers with distinct biological and clinical features. Bibliography 1. Arribas J, Baselga J, Pedersen K, Parra-Palau JL. p95HER2 and Breast Cancer. Cancer Res. 2011;71:1515-9. 2. Christianson TA, Doherty JK, Lin YJ, Ramsey EE, Holmes R, Keenan EJ, et al. NH2-terminally truncated HER-2/neu protein: relationship with shedding of the extracellular domain and with prognostic factors in breast cancer. Cancer Res. 1998;58:5123-9. 3. Anido J, Scaltriti M, Bech Serra JJ, Santiago Josefat B, Todo FR, Baselga J, et al. Biosynthesis of tumorigenic HER2 C-terminal fragments by alternative initiation of translation. Embo J. 2006;25:3234-44. 4. Yuan CX, Lasut AL, Wynn R, Neff NT, Hollis GF, Ramaker ML, et al. Purification of Her-2 extracellular domain and identification of its cleavage site. Protein Expr Purif. 2003;29:217-22. 5. Liu PC, Liu X, Li Y, Covington M, Wynn R, Huber R, et al. Identification of ADAM10 as a major source of HER2 ectodomain sheddase activity in HER2 overexpressing breast cancer cells. Cancer Biol Ther. 2006;5:657-64. 6. Pedersen K, Angelini PD, Laos S, Bach-Faig A, Cunningham MP, Ferrer-Ramon C, et al. A naturally occurring HER2 carboxy-terminal fragment promotes mammary tumor growth and metastasis. Mol Cell Biol. 2009;29:3319-31.

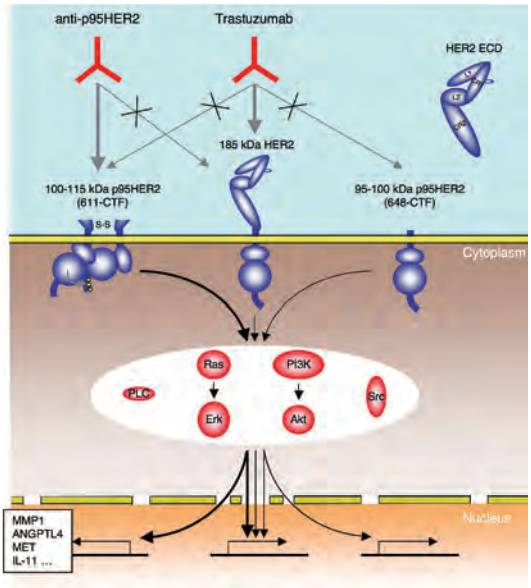

Fig. I

SP06-1

CURRENT STATUS OF ACCELERATED PARTIAL BREAST IRRADIATION (PBI)

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RADIOTHERAPY FOR DCIS

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Detection of DCIS has been increased dramatically since the introduction of screening mammography, and DCIS detection rates around the globe are expected to increase exponentially as women's life expectancy increases and DCIS accounts for 20 to 30 % of incident breast cancers (1).

In DCIS, whole-breast radiotherapy (RT) delivered over 5 to 6 weeks after breast conserving surgery (BCS) reduces the local recurrence rate by approximately 60% and patients with positive resection margins or high-grade DCIS have been shown to benefit the most from adjuvant radiation therapy in terms of prevention of local recurrence (2). Approximately 50% of local recurrences are invasive breast cancer and therefore may be life threatening. Breast cancer mortality following BCS for DCIS is approximately 10% of the overall ipsilateral breast tumor recurrence rate(IBTR) but breast cancer mortality following mastectomy for DCIS is one half IBTR because chest wall recurrence are usually invasive cancers and salvage is approximately 50%. With median follow-up averaging 7 years, IBTR following BCS without RT range from 16-42% and with RT 9-22%. Chest wall recurrence rates following mastectomy range from 0.6-10%.

Following RT for DCIS, tamoxifen reduces the risk of ipsilateral and contralateral breast cancer by 30-50% (3). Although invasive-IBTR (I-IBTR) increased the risk for breast cancer-related death, radiation therapy and tamoxifen reduced I-IBTR, and long-term prognosis remained excellent after breast-conserving surgery for DCIS (4).

Four prospective randomized trials (5-8) have compared BCS to BCS and radiation. These trials have several limitations but the trials are fairly consistent in their results. The addition of radiation decreased the risk of an IBTR by 50-60% with an absolute benefit of 9-16%. Invasive recurrence was decreased by 40% to 50% with absolute benefit of 2-9%. There were no significant differences in survival. It should be noted that the majority of tumors were low grade or non-comedo DCIS in the EORTC trial and the UK/Australian-New Zealand trial was a trial primarily of women greater than 50 years of age, with only 10% less than 50. A Cochrane review of four randomized trials of BCS with or without radiation (3,295 women) reported a 51% decrease in IBTR(invasive or DCIS) with the addition of radiation. There was no increase in non-breast cancer death with radiation and overall survival was similar for the two treatments. The rationale for BCS for DCIS was based on the demonstrated effectiveness of the conservative approach

for early breast cancer. The current challenge is to identify women with DCIS whose risk of an IBTR (primarily invasive) with BCS, with or without radiation and to identify women whose risk of an IBTR after BCS alone maybe low enough to avoid radiation. Based on available evidence obtained from retrospective and prospective trials, all patients with DCIS have potential benefit from radiotherapy after BCS. Further prospective studies are warranted to identify subgroups of low-risk patients with DCIS for whom radiotherapy can be safely omitted. Molecular markers indicating which patients can safely avoid radiotherapy are currently being investigated (9).

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ACCELERATED WHOLE BREAST IRRADIATION (AWBI) IN BREAST CANCER

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Radiation therapy (RT) is proven to play a critical role to reduce loco-regional recurrence for the patients with invasive breast cancer treated with breast conservation surgery (BCS) or mastectomy. Recently altered fractionation schemes such as accelerated partial breast irradiation (APBI) or accelerated whole breast irradiation (AWBI) with hypofractionated RT are actively being tried and adapted in this field. The most commonly used fractionation in many countries including Korea has been 50 Gy in 25-28 fractions delivered over 5-6 weeks with or without a boost to the primary site since NSABP B-06 study in 1985. However because "short course" of hypofractionated schedule for whole breast RT (AWBI) has advantages of patient convenience, lower costs, improved through put for RT departments and ultimately lower health system costs, AWBI regimens have been used at some institutions for many decades. Recent studies have demonstrated that the α/β ratio for breast cancer is low and similar to normal breast, being close to 4 and that the α/β ratio for normal breast tissue is approximately 3.4. There have been four large randomized trials of AWBI assessing the outcome of hypofrationated vs. standard fractionation RT following BCS. These studies are Royal Marsden trial, START A, B and Canadian trials. All these trials showed that the rates of local relapse were equivalent or better among patients treated with hypofractionated AWBI compared to 50 Gy in 25 fractions. They also showed that there was no evidence that patients treated with hypofractionated RT had any worse outcomes of normal tissue side-effects or cosmesis. We, National Cancer Center, performed phase II single arm study of daily 3 Gy, consecutive hypofractionated whole breast (39 Gy) and tumor bed boost RT (9 Gy) for post-BCS breast cancer patients. The dose-fractionation schedule was 48Gy in 16 fractions. The period of patient accrual was between 2006 and 2009, and 277 early breast cancer patients (pTis-2 N0-1 M0) were enrolled. With a median follow-up of 3.5 year (range 2.2-4.8 year), three ipsilateral breast tumor recurrences (IBTR) and four distant failures were detected. The 4-year disease-free and IBTR-free survival rates were 94.6% and 98.0%, respectively. Normal tissue and cosmetic outcomes were evaluated and were comparable. Criticisms against AWBI has focused on concerns about efficacy equivalence, insufficient follow-up of especially normal tissue effects and the lack of data regarding how

to implement the randomized clinical trial data in DCIS patients or those treating RT covering regional lymph nodes. Women with large breasts and the role of boost irradiation when AWBI, are not adequately tested yet. Until now, there are both theoretical and clinical evidence to support the conventional fractionation (50 Gy in 25-28 fractions) does not have the advantage of convenience for patients nor the advantage of a reduced biological effectiveness associated with the extended fractionation schedule. Some clinicians are insisting that conventional fractionation should no longer be the 'standard' for the whole breast RT following BCS.

SP07-1

EFFECTIVE COMMUNICATION ACROSS THE CANCER TRAJECTORY: WHAT PATIENTS CAN TEACH US

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Symposium

Background/Purpose: It has long been recognized that communication is an essential component of effective care for cancer patients. Implicit in the mandate of the health professionals working with those affected by cancer is the requirement for information and support as well as treatment. We know that poor quality or problematic communication in cancer care can have serious consequences for patient and family anxiety and distress, coping, decision making, and overall quality of life. We also know that effective communication makes a powerful positive difference in how cancer patients experience the difficult and often devastating challenge associated with this complex disease and its treatment. When patient advocates and care consumers contribute to policy discussions around improving the quality of cancer care, they consistently emphasize the key role of communication between patients and their professional care providers. Despite the evidence that communication matters greatly in the effectiveness of cancer care, it has been difficult to develop a strong body of empirical knowledge to inform clinical guidelines and best practices for several reasons. First, communication is so inherently complex, particularized and dynamic that it does not lend well to conventional empirical study using measurement to ascertain population patterns or cause and effect relations. Second, cancer is such a complex constellation of different disease experiences. Beyond the known differences in tumour sites and treatment modalities, we recognize that each individual may experience his or her cancer differently at different phases of the cancer journey. Finally, although we have a considerable body of empirical knowledge pertaining to specific pieces of the communication puzzle, it has been difficult to glue them together into a coherent understanding of what patients really need and how we can work toward providing it across our care systems.

Methods: Our program of research has taken a qualitative approach to the study of patient perceptions of their own needs and preferences with regard to communication in clinical care. Recognizing the complexity and diversity of cancer experience, we have worked with larger data bases than is usual in the qualitative context. The methodology

we use draws upon applied disciplinary logic as our theoretical framework, recognizing that knowledge application and transfer to practice are the central mandate of the health disciplines. In our program of research, we have combined both cross-sectional studies and longitudinal cohort investigations. This allows us to detect commonality and diversity across thematic patterns, to test theoretical assumptions against contrary cases, and to track individual variation in perception over time. On the basis of this work, we have come to understand trajectory as a critical feature of experience that has not yet been effectively considered in the attempt to strengthen cancer communication within our systems.

Results: The available research has provided us with useful information about specific "moments" in the cancer trajectory, most especially the time of diagnosis, the delivery of bad news, and the transition to palliative care. We tend to recognize these as times when communication must be sensitively handled. However, our body of knowledge about communication has glossed over other phases within the cancer journey as if routine communication were sufficient to meet the needs. However, patient perspective research by our team and by others makes it clear that communication remains a powerful force, both for harming or for healing, throughout the entire process. There is much to be learned about each phase, and how individuals are changed by time and experience with cancer, that can help us be more mindful in our approach to patient care. Many of the communication problems patients encounter have to do with unintended messages that have consequences beyond the immediate context. An exemplar from our research is the inadvertent distrust in primary care and self-management decision-making that can be germinated by the messaging from members of the specialist oncology care team at the time of diagnosis and treatment decision-making. Through our reassurance and expert knowledge, we create strong confidence in the oncology specialist team and often foster high levels of dependence. However, when initial treatment ends, and patients are referred back into the primary care system, we have not known how to reverse those earlier messages and effectively support their transition into survivorship or chronic management. Similarly, the voices of patients across the cancer spectrum provide us with valuable insights for cancer communication that attends to process and variation, as well as being sensitive to the dynamics of change across time and experience.

Conclusion: Through analysis of patterns and themes in the accounts of patients, qualitatively derived and interpreted through an applied disciplinary logic, we can begin to build a robust body of guidance for practice improvements and enhanced quality of care.

SP07-2

EFFECTIVE COMMUNICATION IN ONCOLOGY ANP OF JAPAN

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I. Situation of oncology society in Japan. In Japan, the leading cause of death has been cancer since 1981 and it continues to be the case because of the rising elderly population and increasing numbers of older people with cancer. In April of 2007, the fundamental law for cancer was legislated. Article 14 of the law states that every cancer patient should have the best medical treatment irrespective of where they live, and maintain a good quality of care. In order to achieve this, a multidisciplinary oncology professional team is needed to offer quality care to patients and families. As a result, an oncology training program for health-care professionals such as physicians, nurses, pharmacologists, and radiologists has been developed. The project began in 2007 and will run for five years until 2012. II. Situation of oncology certified nurse specialist (OCNS) as advanced nursing practice (ANP). For nurses, there is the training program of OCNS as ANP. Actually, the OCNS training program has been in existence since 1996 at master's level of graduate school. But since the project started in 2007 the number of graduate schools of nursing and students offering the program has been increasing rapidly. For example the number of schools running the OCNS programs was 11 in 2007 and has increased to 44 in 2011. The number of OCNS was 79 in 2007, and 250 in 2011. The plan is for there to be 500 OCNSs within the next few years. In order to take the certified examination offered by the Japanese Nursing Association, there is a requirement of over six months of clinical practice following completion of the training program, as well as a history of more than five years clinical practice of which three years must be in cancer nursing. As to the roles of ANP, OCNS focuses on clinical practice in meeting the health needs of individuals, families, groups, and communities. It involves analyzing and synthesizing knowledge, understanding and applying nursing theory, doing research, and developing nursing knowledge. And Japanese OCNSs carry out the following roles. 1) Efficiently providing a high level of nursing care to individuals, families, groups, and communities (clinical practice). 2) Having educational function to make general nurses improve cancer care (education). 3)Consulting to care givers including nurses (consultation). 4) Coordinating among health care professionals in order to manage smoothly necessary care (coordination). 5) Doing research in the clinical field to improve and de-

velop nursing knowledge and skill (research). 6) Doing ethical coordination among people who face ethical problem and conflict (ethics). III. Effective communication of OCNS. < Basic communication skill > Effective communication is a component of the professional practice role of OCNS, as it exerts an influence on patient's outcomes. Communication in cancer care is challenging due to fear and stigma associated with cancer, complexity of medical information and uncertainty about the course of the disease. The followings are the elements for communication skill. 1) Trust: Building trust with patients and families is most important to effectively communicate. Without trust, communication may break down, and your advice or information may be disregarded. Trust increases when communication is honest. 2) Empathy: Patients might be scared, angry or frustrated to find themselves under medical care. So it is necessary to offer empathetic statements respecting patient dignity. Respectful communication will be more effective than cold or gushy dialogue. 3) Listening: Active listening is important for effective communication. For example, in cases of patients, families or coworkers complain, or feeling lost or unheard in busy medical settings. In order to confront difficult issues, active listening is more useful than speaking or any other form of expression. 4) Nonverbal: Effective communication relies not only on speaking and listening, but also body language such as direct eye contact, lower your body position not to talking down, or physical touching if appropriate. 5) Documenting: Communication should be documented and shared for patient care with staff. Failing to communicate important change in patient status, behavior or attitude might result in misdiagnosis or errors in care. Written communication should be legible, listed in chronological order, dated and signed. < Communication as OCNS > OCNS takes responsibility for their patient's health care needs and arrange care with other health-care professionals as needed. Thus OCNSs communicate with multidisciplinary care team members in order to coordinate and integrate a patient's care. Collaboration in the form of effective communication complements the delivery of health care. The followings are the elements for OCNS to communicate. 1) Communicating effectively and sharing knowledge, skill and expertise with other health-care professionals as required for the benefit of patients and families. 2) Continuously analyzing and improving level of communication skill in encounters with patients, families, and health-care professionals. 3) Choosing communication styles that diminish the risks associated with authority gradients among multidisciplinary care team members.

SP07-3

COMMUNICATION BETWEEN HEALTH CARE PROVIDER AND PATIENTS

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SP07-4

CONVERSATION ANALYSIS TO IMPROVE ONCOLOGY NURSING COMMUNICATION

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The purpose of this presentation is to provide a brief review about conversation analysis and how it could improve communication between cancer patients and oncology professionals, specifically oncology nurses.

Communication is an essential element in health care, as quality of health services depends largely on the quality of communication. It is growing more important nowadays because patients are more engaged in their medical decision-making process and they are more accountable to their health. Thus, equal partnership, with cooperation between patient and health professional, is emphasized and encouraged in contemporary health care settings.

Conversation analysis (CA) deals with talk-in-interaction; that is, naturally occurring data. Its purpose is to get a clear picture of *in situ* organization by identifying detailed and patterned organization of interactions in natural settings. CA has a few basic assumptions. First, talk is systematically organized and deeply ordered. In other words, each participant orients in their own order when understanding another's action. Second, order is repeated and recurrent. Thus, the purpose of CA is to discover and describe the produced orderliness in the task. The central feature of CA focuses on the turn-by-turn unfolding of talk-in-interaction.

Existing conversational analytic studies in medical interactions have focused on clinical and institutional encounters involving health professionals and patients. It is known that doctor-patient interaction is asymmetrical, because roles and tasks are different between doctors and patients. Some problems occurring in this asymmetrical communication are discussed in the literature. However, very few studies have examined encounters between nurses and patients.

In the studies of conversation between nurses and patients with dementia in a geriatric setting, four functional phases were identified: introduction; assessment; intervention;

and closing. In the assessment phase, three sequential patterns of nurse-initiated dialogue and four sequential patterns of patient-initiated dialogue were identified. In the intervention phase, four sequential patterns were identified in nurse-initiated and three in patient-initiated dialogues. In general, 'inquiring of condition of the patients', 'advising', and 'giving directions' were the most frequent kinds of dialogue by nurses, indicating the nurses' domination of the conversation. At the same time, 'asking back', 'refuting,' 'escaping from bothersome questions', or 'giving false promising' were used often by nurses to discourage patients of talking when the patients were raising questions or being demanded. In the analysis of communicative problems, 'directive and authoritative expressions', 'emotional and competitive expressions', 'evasive and on-looking expressions', and 'excessive use of title only', such as calling them granny or grandpa instead of their proper names were identified as problematic expressions. 'Lack of themes in psychosocial areas' and 'nurse-led relations' were identified respectively as communicative problems in terms of content and relationships. In the analysis of non-verbal communication with 66 episodes of the same data, patient-directed eye gaze (94%) was the most frequently used type among nurses followed by affirmative head nodding (67%) and forward leaning (67%), while smiling was the least used (32%) among seven nonverbal categories. Affective touch was identified in 39 episodes (59%). There were wide differences among nurses in terms of using affective touch, ranging from 0% to 98%. Also nonverbal behaviors were more frequently identified in effective episodes than in ineffective episodes.

These results suggest that communication between nurses and patients is asymmetrical, nurses dominating as in doctor-patient communication. But, further CA studies are needed in encounters between nurses and cancer patients to provide substantial guidelines for nurses in caring for cancer patients in various situations, such as admission, discharge, medication, or other nursing intervention for pain, discomfort or other issues. The organization of conversation in these specific situations would provide formal resources to accomplish interactional tasks, and deploys these resources in a manner that is sensitive to just what circumstances and participants happen to be at hand. In conclusion, the results of CA could help improve the quality of health services by promoting equal partnerships through deep understanding of linguistic structures and identifying problems of everyday conversations between nurses and cancer patients.

SP08-1

TRIPLE NEGATIVE BREAST CANCER: PATHOLOGIC AND MOLECULAR FEATURES

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Breast cancer is a complex and heterogeneous disease with varied morphological appearance, molecular features, behavior and response to therapy. The triple negative breast cancer (TNBC) is a particular type of breast cancer defined by absence of estrogen (ER) and progesterone receptor (PR) expression as well as absence of human epidermal growth factor receptor-2 (HER2) gene amplification. It represents approximately 10-20% of all breast cancer cases, depending on the thresholds for ER and PR positivity and the HER2 assessment method, as well as the age and racial groups. In Korea, TNBC accounts for 20.3% of all invasive breast cancers when definition of HER2 and hormone receptor positivity of ASCO/CAP guidelines and silver-enhanced *in situ* hybridization technique for HER2 testing were applied on 1,198 samples. TNBC is more prevalent in younger patients (< 50 years), African-American women and BRCA1 mutation carriers. It associates with an aggressive clinical course with peak risk of recurrence in the first 1-3 years and majority of deaths occur in the first 5 years. Other clinical implications of TNBC are that there is a lack of tailored therapy for this group of patients, such as hormone therapy and HER2-targeted therapy and that there is a significant overlap between TNBC and basal-like breast cancer (BLBC). It is important to recognize that the designation of TNBC is based on clinical assays for ER, PR and HER2; whereas BLBC is a molecular phenotype initially defined using gene expression profiling (cDNA microarrays). The histological hallmarks of TNBCs are high grade, high proliferative activity, geographic necrosis, a pushing border of invasion, presence of central scar/fibrotic foci and prominent lymphoplasmacytic inflammatory infiltrate. However, most of the histological features of TNBC are not specific and are observed in other high-grade tumors. TNBC has an increased propensity for visceral metastases to brain, liver and lung. Most TNBC (80-90%) is poorly differentiated ductal carcinoma of no special type but other high and low grade histologic types such as medullary, metaplastic, apocrine, secretory and adenoid cystic carcinomas comprise the rest of TNBC. Although somatic mutations in BRCA1 have not been detected in sporadic TNBC, BRCA1 protein dysfunction by promoter hypermethylation, LOH of BRCA1 and ID4 overexpression was observed in a subpopulation of TNBC, which provides therapeutic opportunity by poly (ADP-ribose) poly-

merase (PARP) inhibitors in patients with TNBC. Genome-wide analysis of TNBC aims to develop novel prognostic and predictive biomarkers and effective therapeutic targets. By gene expression profiling, TNBC is subclassified into basal-like, HER2-enriched, claudin-low, luminal B, luminal A and molecular apocrine subtypes. BLBCs express genes characteristic of basal or myoepithelial cells, including basal cytokeratins (CK5/6, CK14, CK17), P-cadherin, caveolins 1 and 2, nestin, αB crystalline, and epidermal growth factor receptor (EGFR). A previous study showed that 71% of TNBCs were of basal-like subtype by gene expression profiling. Therefore the main characteristics of BLBC have similarities to those of TNBC in clinical presentations, histological features, response to chemotherapy, sites of distant relapse and outcome. Although several immunohistochemical surrogates have been proposed for BLBCs, including triple negative phenotype, ER-HER2 negative (double negative) status, expression of one or more basal cytokeratins and lack of expression of ER and HER2 with expression of CK5/6 and/or EGFR, there is no internationally accepted definition or consensus for BLBCs. Therefore, BLBCs are still a poorly characterized subgroup of breast cancers and there is a possibility that BLBCs defined by other groups consisted of quite heterogeneous population of breast cancers. Claudin-low subtype is characterized by the lack of expression of claudin-3, claudin-4, claudin-7 and E-cadherin, but enriched for markers that are linked to stem cell function and epithelial-to-mesenchymal transition, which are important for tumor metastasis. Claudin-low tumors have similar survival curves as other poor prognosis subtypes such as luminal B, HER2-enriched and basal-like subtypes. In contrast to BLBC, claudin-low tumors are associated with lower expression of proliferation genes. The molecular apocrine subtype is a group of non-basal ER-negative breast tumors with increased androgen signaling. It has strong apocrine features such as abundant eosinophilic cytoplasm and prominent nucleoli and androgen receptor positivity. The apocrine subtype comprises of less than 5% within the TNBC. I would like to review subtype specific molecular and clinical characteristics of TNBCs with an emphasis on BLBCs. Understanding the biology of TNBC is essential for the development of effective therapeutics.

SP08-2

NEW STRATEGIES FOR TREATMENT OF TRIPLE NEGATIVE BREAST CANCER

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INTRODUCTION

Breast cancer is not considered anymore a unique disease. Microarray gene expression analysis led to the identification of 4 major breast cancer "intrinsic" subtypes, including hormone receptor (HR)-positive luminal A and B, human epidermal growth receptor 2 (HER2)-positive and basal-like breast cancer. These subtypes have distinct phenotypes, molecular profiles, clinical behavior and response to therapy. The triple-negative breast cancers (TNBC) are defined by a lack of expression of estrogen, progesterone, and HER2/neu receptors at IHC analysis. These tumors account for approximately 15% of breast cancers. Histologically and transcriptionally, TNBC have many similarities to BRCA1-associated breast cancers, which suggests that dysfunction in BRCA1 or related pathways occurs in this subset of sporadic cancers. Clinically, they occur in younger women as interval cancer, and the risk of recurrence is higher within the first 3 years. Distant recurrences in the brain and visceral metastases are more common than in HR-positive tumors. Current chemotherapeutic treatments for TNBC include anthracyclines, taxanes, combination of ixabepilone-capecitabine and platinum agents. Despite being highly chemosensitive, their progression-free time is generally short. Given the lack of common therapeutic targets, TNBC represent a major challenge for breast oncologist. In this review, I will summarize the updated knowledge on TNBC, with emphasis on the new therapeutic options under development.

NEW THERAPEUTIC STRATEGIES

1. Platinum salts

A key issue is th e role of platinum salts because of their specific mechanism of action, in that they cause DNA cross-link strand breaks. In cells that lack homologous repair, such as BRCA mutants, and possibly in BRCA-deficient cells, this could be a particularly effective treatment approach. In several small clinical trials, platinum derivative have shown promise, but their use is not supported yet by randomized evidence and

should therefore be limited to clinical trials.

2. Bevacizumab

The E2100 phase III study (paclitaxel ± bevacizumab) showed benefits of paclitaxel in combination with bevacizumab as first-line treatment in metastatic breast cancer. This study included a vast majority of HER2-negative patients (91%) and the triple-negative subgroup also showed clear advantages with the addition of bevacizumab. Two additional studies demonstrated increased objective response rates with the addition of bevacizumab in metastatic cancer (AVADO and RIBBON-1 study). However, there is no clearer signal that this antiangiogenic agent has any special properties in the triple-negative cohort compared with the broader population. There are ongoing protocols that have included this monoclonal antibody in different adjuvant chemotherapy regimens in only TNBC (BEATRICE) or only HER2-negative tumors (CALGB 40603), as well as phase II trials in TNBC patients in the neoadjuvant and metastatic settings.

3. PARP inhibitor

DNA repair pathways are vital for maintaining genome integrity, and the most important pathways involved in DNA repair include double strand break (DSB) repair, base excision repair (BER). BRCA1 and BRCA2 play an important role for DNA DSB repair by homologous recombination (HomR) and mutations in these genes have been linked to the pathogenesis of hereditary breast cancer. As widely described in literature, BRCAness is common feature between TNBC either hereditary or sporadic. PARPs (poly [ADP-ribose] polymerases) is a superfamily of highly conserved 17 enzymes and PARP1 is essential for DNA SSBs repair by sensing the presence of SSBs and by recruiting BER multiprotein complex at the damaged DNA site. PARP inhibitors are specific inhibitors of PARP-1 and consequently of the DNA SSBs repair system. On the basis of initial findings, preclinical investigators proposed that a PARP inhibitor would be especially useful as a single agent, or in combination regimens in patients with BRCA mutations. In the phase II study with olaparib, an oral PARP inhibitor, 63% of patients experienced clinical benefit. While olaparib was evaluated exclusively in BRCA1/2 mutated tumors, Intravenous BSI-201 have recently been presented in the more general setting of TNBC in a randomized phase II study (table). Preliminary results with PARP inhibitors in TNBC show great potential. The impressive phase II results with the PARP inhibitors have led to a definitive phase III study involving more than 420 patients.

FUTURE DIRECTIONS

TNBC has no known specific target so far and is usually considered an aggressive treatment-resistant disease. However, a large number of therapies have been developed to date for specific molecular targets used as monotherapy or combined with traditional chemotherapy. Currently there are over 50 clinical trials assessing various therapeutic options. Improved knowledge of the role of BRCA1 and the discovery of metabolic pathways has led to the development of other therapeutic strategies. Preliminary results with PARP inhibitors are particularly exciting. Also, anti-angiogenic drugs and EGFR inhibitors may play a role in this rapidly evolving therapeutic scenario.

SP08-3

PPAR GAMMA REGULATES TUMOR-SPECIFIC REPRESSION OF MNSOD EXPRESSION

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Ligand induced peroxisome proliferator-activated receptor gamma (PPARγ) activation has been reported to inhibit the proliferation of malignant cells, possibly through reactive oxygen species (ROS) production. An increasing number of studies have demonstrated that elevation of cellular ROS can indeed kill cancer cells more effectively. Compelling evidence suggests that cancer cells are generally under oxidative stress, which renders them more dependent on superoxide dismutases (SOD) to protect them. Manganese superoxide dismutase (MnSOD) is one of the major antioxidant enzymes that could regulate ROS-mediated cell death induced by PPARγ activation. Recently, a strategy termed 'oxidation therapy' has been coined using ROS-inducing approaches to target cancer cells and increase their chemo-sensitivity to anti-cancer drugs. We report the identification of human MnSOD as a PPARγ target gene and that activation by PPARγ agonists led to downregulation of MnSOD mRNA and protein levels. Importantly, normal breast cells were completely refractory to this effect. Furthermore, MDA-MB-231 xenograft model in nude mice treated with PPARγ ligands showed significant reductions in tumor size, and tumor tissues stained by immunohistochemistry showed a decrease in MnSOD protein levels. A histopathologic analysis of breast cancer biopsies obtained from patients treated with synthetic PPARγ agonists showed MnSOD repression. With MnSOD repression, a corresponding increase in intracellular superoxide production in breast cancer cells was observed upon PPARγ activation, which did not occur in normal breast cells. Suppression of MnSOD levels by small-interfering RNA or PPARγ agonists in breast cancer cells increased oxidative stress and enhanced chemo-sensitivity to ROS-inducing drugs such as docetaxel and doxorubicin. Together, our data not only identifies MnSOD as a novel target of PPARγ but also provides a molecular mechanism for ROS-manipulation therapy in the clinic through the intelligent use of PPARγ ligands in combination with ROS-inducing drugs such as doxorubin or docetaxel.

SP09-1

INDIVIDUALIZED OVERALL TREATMENT PROGRAMS FOR PATIENTS WITH LOCO-REGIONAL RECURRENCE

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Locoregional recurrence (LRR) after the initial treatment for breast cancer is not uncommon. About 10% to 20% of these recurrences are isolated locoregional recurrences, while 60% to 70% are distant metastases in one anatomical structure or else in multiple locations. Although there are relatively well established guidelines for the initial treatment for breast cancer, treatment recommendations are not as well defined after LRR. Literally, LRR is composed of local recurrence and regional recurrence, but the discrimination of 'local' and 'regional' is not easily possible. The pattern of LRR is different according to the initial local treatment, i.e. mastectomy or breast conserving surgery with or without radiation. It also often has simultaneous or antecedent distant metastases. It is sometimes really challenging to judge that it is isolated LRR or a prodrome of systemic metastasis once LRR has occurred.

According to the hypothesis of the breast cancer spread, there are three theories regarding the clinical behaviour of LRR of breast cancer. The first one is the Halstedian theory which proposed that breast cancer begins as a strictly local disease and that tumor cells spread over time in a contiguous manner away from the primary site through lymphatics. The second one is the systemic theory which suggests that breast cancer is a systemic disease from the time of primary diagnosis and factors such as axillary lymph node status and LRR are markers of risk rather than the source of distant metastases. If a patient's overall survival is dependent on the distant metastasis, the control of LRR is of little value. However, both Halstedian theory and Fisherian theory are not correct since the evidence from randomized clinical trials supporting a link between local control and overall survival in breast cancer. The third one is "alternative" or "spectrum" theory which proposed that breast cancer is a heterogeneous disease, a spectrum of from a disease that remains local throughout its course to one that is systemic when first detectable. It is really a tough challenge for breast care physicians since the treatment of LRR can be beneficial or useless according to the individualized situation.

The pattern of LRR is distinct according to the types of initial surgery. Although there has been few data about the management of specific sites of LRR, the treatment of LRR can be broadly divided into local and systemic therapy. Local therapy includes surgical resection and radiation therapy. Systemic therapy can be combined, and chemotherapy, hormonal therapy and targeted therapy can be considered.
For patients initially treated with breast conserving surgery, most subsequent local recurrences occur within the ipsilateral breast tissue. About 90% of these ipsilateral breast tumor recurrences are surgically operable by salvage mastectomy. Conservative re-excision without radiotherapy does result in a poorer outcome. Although radiation therapy is a common LRR treatment option in those who have not post-mastectomy radiation therapy, it is challenging for the patients who already had potentially curative doses of more than 50 Gy, since the cumulative radiation dose may deliver severe toxicities. Five-year overall survival after an ipsilateral breast tissue recurrence it is almost 80%. The second most common site of LRR is axillary lymph nodes. Patients with negative nodes at the primary breast conserving surgery have an 8% incidence of distant metastases at the LRR, compared with 36% for those with 1 to 3 positive nodes, and 50% for those with 4 of more positive nodes.

For patients initially treated with mastectomy, surgical excision from simple excision for the small subcutaneous recurrence to extensive surgery for the isolated chest wall recurrence can be considered. Regarding to radiation therapy, there was a retrospective study comparing limited surgical excision, radiotherapy, or limited surgical excision followed by radiotherapy for chest wall recurrence after mastectomy showed the chest wall recurrence rates after each treatment were 62%, 83% and 30%, respectively.

In consideration of treatment for the LRR, one must think over the potential benefit from the local treatment. According to the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis, there was one more death from breast cancer at 15 years for every four LRR patients at 5 years. It means one of four LRR is related to the systemic spread of the breast cancer, leading to an increased risk of death from metastatic disease. Unfortunately, who will be "the one in the four LRR" is inconclusive yet. The time from the initial treatment to LRR, receptor conversion in breast cancer recurrence should be also considered for the treatment of patients with LRR with local or systemic therapy or both.

For operable breast, chest wall, and axillary recurrences, excision can be strongly deliberated with tumor-free margins. For ipsilateral breast tumor recurrences after breast

conserving surgery and radiation, mastectomy is regarded as the standard treatment. In selective cases, breast conserving re-excision can be cautiously considered. Systemic therapy (chemotherapy, hormonal therapy, targeted therapy, bisphosphonates, or combination of these) can be applied according to the molecular characteristics of recurred tumor in high suspicion of prodrome of systemic metastasis.

MANAGEMENT FOR IPSILATERAL BREAST RECURRENCE AFTER BREAST CONSERVATION TREATMENT

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Background: Breast conserving operation has been a standard treatment for early breast cancer since 2003 in Japan. About 60% of the patients underwent breast conserving operation in 2009. About five to ten percent of them developed ipsilateral breast tumor recurrence (IBTR). Relative incident of IBTR is low but the absolute amount is high. So it is an important issue how to manage IBTR. Indeed, many issues remain to be elucidated. We report here the actual conditions of IBTR, predictive factors of IBTR, relationship to the prognosis, and the factors which can predict outcome.

Patients and Methods: Fifty six patients with IBTR among 1,372 patients treated by breast conserving operation between 1988 and 2005 at Keio University Hospital were analyzed in the first series. Second series consist of 1,901 patients who underwent breast conserving treatment at 18 Japanese institutions between 1986 and 1993. Third series is a total of 172 patients with IBTR. Patients with IBTR were classified as true recurrence or new primary based on tumor location and pathological findings.

Results: In the first series, 56 patients (4.1%) developed IBTR with median follow up of 73 months. Local control rate was significantly lower in younger age group, larger tumor size, without radiation and/or adjuvant systemic therapy. Salvage mastectomy was performed in 55% of the cases. Re-breast conserving treatment was performed in 30% of the patients. Three year survival rate was 87.1%. Overall survival was not significantly different between two groups. Lymphatic infiltration at the recurrent tumor was a significant prognostic factor. The patients with the tumor recurred in the same quadrant of the original one showed a poorer prognosis compared to the patients with the tumor recurred in the other quadrant. Results of the second series showed that the 10-

year overall survival and disease-free survival rates were 83.9% and 77.8% respectively at a median follow-up of 107 months. The 10 year cumulative rates of IBTR rate were 8.5% in the patients with postoperative irradiation and 17.2% in the patients without irradiation. IBTR significantly correlated with subsequent distant metastasis ($p < 0.0001$). Among patients who developed IBTR, initial lymph node metastasis and short interval to IBTR were significant risk factors for subsequent distant metastasis. In the third series, 135 patients were classified as true recurrence and 26 as new primary. Eleven cases could not be categorized. The five-year survival rates after IBTR were 71% in true recurrence and 94.7% in new primary ($p = 0.022$). Salvage operation was performed in 136 IBTRs. Eighty-one patients underwent salvage mastectomy and 55 patients underwent repeat lumpectomy. Five-year survival rates after salvage operation were 75.7% for mastectomy and 84.2% for lumpectomy (N.S.). Twenty percent of patients who underwent repeat lumpectomy developed secondary local relapse within 5 years after salvage treatment.

Conclusion: IBTR occurred about one tenth of the patients with breast conserving operation. Methods of salvage operations did not significantly affect prognosis, although IBTR per se is a factor predicting poor prognosis. To manage IBTR, it is mandatory to differentiate true recurrence from new primary.

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SYSTEMIC TREATMENT STRATEGIES IN METASTATIC DISEASE: CHEMOTHERAPY, ENDOCRINE THERAPY AND BIOLOGIC THERAPY

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Breast cancer cases in western country showed that 60 % were approximately detected in early localized stage (-however more than 20 to 30 % will develops recurrent and metastatic disease-); 30 % were in regional stage (- spread to the regional lymph nodes or beyond primary site-) and only less than 10% were in metastatic stage, at which point the disease is incurable. Our data in Darmais and Cipto Mangunkusumo hospital, showed that on between 2001-2005, around 60-70% patients were come with locally advance and advance stage. Five year survival rate of metastatic breast cancer (MBC) compared to early and localized stage is still poor: 27%, 98%, and 84% respectively; with median survival of 2 to 4 years. The goal of treatment in MBC is to relief symptoms, maintain and improved quality of life and prolongation of survival; up to recent years there is no standard of treatment in MBC; that is why the strategy of treatment to choose the first, second line of treatment and beyond; is important. Patients and tumor characteristics (- like patient performance, co-morbid, disease free interval, previous chemotherapy agents, sites and number of metastases involvement, aggressiveness of the disease, tumor biomarker -) should be used to support individualized approach of treatment.

Patients with less aggressive, immediately not life threatening and ER, PR or both positive (- or not known hormonal status but with less aggressive characteristic -), endocrine therapy is generally better tolerated and amenable as 1st line of therapy than cytotoxic chemotherapy. Premenopausal MBC patient can proceed with anti estrogen (tamoxifen) and ovarian suppression or ablation therapy; but not in post menopausal patients in which aromatase inhibitor was recommended as first-line treatment, with tamoxifen remaining to constitute a valuable option. Endocrine therapy should be continued until the patients have disease progression or unacceptable toxicity.

Patients with negative hormone status or not response or relapses during or within one year after ajuvant hormone therapy should be offered for primary chemotherapy. Candidates for chemotherapy are also patients with bulky visceral disease, severe tumor-related symptoms or rapid progression, irrespective of hormone receptor status. How do

we proceed? Do we have to used single agent or combination cytotoxic agent ? Compared with single-agent chemotherapy with old nonanthracycline (- like cyclophospamide, vincristine, 5FU, methotraxate -) drugs, anthracycline regimens achieved 22%-33% relative risk reductions in mortality, (hazard ratio [HR], for standard-dose anthracycline-based combination: 0.67 [0.57-0.78]) Several newer regimens achieved further benefit, 0.67 (0.55-0.81) for single-drug taxane, 0.64 (0.53-0.78) for combination of anthracyclines with taxane, and 0.49 (0.37-0.67) for taxane-based combination with capecitabine or gemcitabine.

At the onset and during chemotherapy, an assessment of cancer-related symptoms and performance status should be carried out and have to be recorded with each cycle. To avoid continuing ineffective therapy, tumor response should be assessed every two or three cycles. In the field of biology therapy , traztuzumab represent an effective anti Her-2 receptor in patients with over expression of Her-2 receptor in which cover 20-30% of MBC. It can be use alone or in combination regiment. Studies showed an additive and even synergistic activity traztuzumab with a range of cytotoxic chemotherapy agent. Slamon et al in a pivotal phase III 1st line therapy, compare three weekly chemotherapy with traztuzumab (weekly) vs chemotherapy alone (paclitaxel or doxo-cyclo or epi-cyclophospamide.) Results showed that group with additional traztuzumab have significantly higher RR; longer TTP ($p < 0,001$) and increase median OS by 5 months ($p = 0,046$). This studies also showed combination with anthracycline base therapy, have significantly higher cardiac toxicity. Robert et al in another phase III 1st line with an additional non anthracyclin combination regiment consisting paclitaxel-carboplatin-traztuzumab vs paclitaxel-traztuzumab alone showed increased PFS 10,7 vs. 7,1 months in carboplatin group. ($p = 0,03$). Other combination with taxanes ,vinorelbine, capecitabine also yielded benefits. Another biology agent is lapatinib with dual epidermal growth factor receptor (EGFR) and HER2 inhibitor. Lapatinib was approved in USA combined with capecitabine in patients already exposed to taxanes, anthracyclin and traztuzumab; and showed significantly more effective than capecitabine alone.

Anti angiogenesis bevacizumab (BEV) was tested in combination with capecitabine, taxane and anthracyclin base therapy on phase III RIBBON-1 study and with docetaxel in HER2 negative phase III AVADO trial. Both studies showed significant longer PFS but not in OS in BEV combination group.

Regarding systemic therapy in MBC, an important consideration is the balance between the benefit of treatment and the harms or adverse effects that these treatments may have.

SP10-1

BUILDING EVIDENCE IN ONCOLOGY NURSING CARE

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Recent academic attention on evidence based practice (EBP) pushes us to rethink what we have done and whether or not we have known what we are doing to patients as oncology nurses. Searching for the rationale in our merrily practice and building so called new evidence according to the evidence ladder are imperative and urgent tasks for any of us. In nursing, however, the paradigmatic and philosophical commensurability of the notion of 'evidence based practice' should be reconsidered since not only positivistic aspects but relativistic features in terms of the process and outcomes of nursing exist remarkably.

It is then argued that the notion of EBP shorts to embrace the outcomes of oncology nursing in all aspects, given the breadth and depth of the body of nursing knowledge and practice on care for cancer patients. In this presentation, the incommensurable aspects within oncology nursing compared with the EBP nomenclature will be compared and contrasted. Also, the incongruity of the EBP pyramid when it is applied as a method for building authentic evidence in oncology nursing will be discussed. Then, the strategies to incorporate quantitative and qualitative research evidence into practice will be presented with the exemplars in the author's program of research. Upon this presentation, the cautious reevaluation on EBP and constructing the innovative ways of accumulating evidence in oncology nursing in all academic and practice areas are wished to be provoked.

SP10-2

MENOPAUSAL SYMPTOM MANAGEMENT IN PATIENTS WITH BREAST CANCER

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This presentation will summarize the current evidence surrounding menopausal symptom management in patients with breast cancer. Objectives are to describe menopausal symptomatology in breast cancer; evaluate the evidence surrounding treatment options and treatment decision making; and discuss future directions for research and practice.

Menopause affects all women who live to reach mid-life. During menopause, most women experience two or more concurrent menopausal symptoms including vasomotor symptoms (hot flashes, night sweats), depressed or anxious mood, sleep disturbances, and/or sexual difficulties. Up to 75% of women report seeking help from a health care professional for menopause, and in the United States, median annual health care expenditures for midlife women are 55% higher than for midlife men. The incidence and severity of menopausal symptoms are known to vary by menopausal stage, racial/ethnic group, sociocultural factors, clinical characteristics, and geographic region.

Women with breast cancer are at high risk for menopausal symptoms due to therapeutic estrogen ablation. The clinical presentation varies by age with premature menopausal symptoms seen in young women, re-emergence of symptoms seen in older postmenopausal women, and exacerbated symptoms seen across age groups. Breast cancer patients can experience hot flashes due to chemotherapy, selective estrogen receptor modulators (e.g., tamoxifen) or aromatase inhibitors (e.g., letrozole). In addition, abrupt discontinuation of hormone therapy at the time of breast cancer diagnosis can contribute to symptoms. As a result, menopausal symptoms are more frequent, severe, and distressing for breast cancer patients in comparison to women without cancer of the same age.
Hormonal therapies are contraindicated for breast cancer patients so other non-hormonal therapies are typically recommended. These have included non-hormonal biologics (medications, herbs, vitamins), energy therapies (acupuncture), physical activity (exercise, yoga), and cognitive-behavioral interventions (relaxation, paced respiration, self-hypnosis, mindfulness-based stress reduction). Many of these therapies have not been rigorously tested, or if tested have a limited evidence base, are unacceptable, or are

only partially effective for breast cancer patients. Few therapies result in a 50% or greater reduction in VMS - the median amount of relief desired by women and the difference needed to improve women's quality of life. There is little evidence for multiple concurrent treatments or stepped care treatments, even though these may be commonly used in clinical practice.

Our understanding of how breast cancer patients make menopausal symptom management decisions in the context of these far ranging treatment options is also limited. Up to 80% of midlife women (including breast cancer patients) talk to a health care provider about menopausal symptom management options, yet most do not feel fully informed and have concerns about various options. For example, a survey of 781 midlife women revealed that 75% did not feel fully informed about herbal products, 64% had concerns or were not sure about herb-drug interactions, and 61% did not feel confident about herbal product dosing. In another survey, nearly half of 293 women reported feeling confused about menopausal symptom management treatment options. Although acceptability, cost, side effects, and efficacy may be concerning to all women, there are additional special issues for breast cancer patients such as contraindications to hormone therapy, possible tumor-promoting effects of botanical products, and prescription treatments that interfere with endocrine therapies. Although the majority of breast cancer patients would prefer to receive menopause information via a decision aid or one-to-one consultation, there are no such existing decision aids for breast cancer patients. Decision aids are tools to facilitate informed decision making. Currently available menopausal decision aids are limited in number and focus on hormone therapy or natural health products (herbs, vitamins) and, therefore, are not appropriate for breast cancer patients. A menopausal symptom management decision aid would be beneficial for breast cancer patients because such aids have been shown to increase patients' knowledge, reduce patients' decisional conflict, increase patients' decisional satisfaction, and help prepare patients to engage in shared decision making with health care providers.

The key steps for the future are to (1) carefully implement the existing evidence base into clinical practice and evaluate resulting changes in patient outcomes and (2) continue to generate the evidence base needed to guide treatment and treatment decision making. Because a lack of understanding of menopausal symptomatology is a major barrier to identifying novel treatments, a combination of basic and clinical sciences is needed to build the evidence base for practice. In addition, decision aids need to be developed, tested, and implemented to help guide women through the myriad of treatment choices so that their menopausal symptomatology is addressed and their quality of life is improved.

SP10-3

EVIDENCE-BASED ONCOLOGY NURSING PRACTICE IN KOREA

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Evidence based practice (EBP) is the integration of clinical expertise, patient values, and the best research evidence into the decision making process for patient care (Sackett, 1996). EBP process consists of 5 steps of asking the clinical question (PICO), searching for the best evidence, critically appraising the evidence, integrating and implementing, and evaluating the outcome of evidence implementation. Many institutions including Cochrane collaboration (www.cochrane.org), National Guideline Clearinghouse (http://www.guideline.gov), and Joanna Briggs Institute (JBI) are providing clinicians with standardized guidelines and best evidences. National Comprehensive Cancer Network (NCCN) is providing practice guidelines in oncology care. And Oncology Nursing Society Putting evidence into practice (ONS PEP) resources provide quick references for effective evidence-based nursing interventions. Many hospitals are operating RN-driven EBP project teams and providing organizational support for the teams. In Korea, however, the first conference on EBP was held by Korean Academy of Nursing in 2004, thereafter a few symposia were held by academic societies and hospitals. The EBP activities by clinical nurses started actually in 2009. And recently the Korean Society of Evidence Based Nursing (KEBN) was founded in January 2011. According to one Korean study, nurse's perception of the importance of EBP and perceived organizational support were relatively high, but limitation in knowledge on research language and statistics and lack of time to devote to EBP were barriers in EBP. When needing help for decision making clinical nurses refer to literatures, but reading article was not sufficient, as they were not familiar with reading articles and interpreting the data. Another study by Korean Hospital Nurses Association (2011) reported many clinical questions which, nurses think, need to be improved. According to the study, frequently asked questions related to oncology nursing practice were on 'management of central venous catheter', 'administration of chemotherapeutic agents', 'reverse isolation', 'oral care', and 'pain management'. And high priorities for developing practice guidelines were put on the subjects such as pain management, medication administration, intravenous drug therapy, management of central venous catheter, and transfusion. Few clinical practice guidelines on oncology nursing were published in Korea. The only guideline developed by

Korean Oncology Nursing Society was guideline on the chemotherapy administration and management of central venous catheter. Survey on the priorities of developing guidelines in oncology nursing in Korea was not successful, for oncology nurses did not have enough understanding in EBP and PEP guide developed by ONS. But recent EBP movement driven by tertiary hospitals and foundation of KEBN are promising. These activities will be good stimuli for nursing society, including oncology nurses to participate in EBP more actively. Although there are few researches on nurse's readiness for EBP and priorities for practice guideline for oncology nursing exclusively in Korea, some suggestion can be made. For activating the EBP in oncology nursing in Korea, oncology nurses should be accustomed to research methodology, statistics, and EBP through education and participating in research or EBP. In addition, nurses should afford to devote time for EBP with organizational support. Korean Oncology Nursing Society (KONS) should play a great role in developing oncology nursing practice guidelines and expanding evidence-based nursing practice. During the process active participation of the oncology APN is imperative.

SP11-1

DISTRESS OF ALTERED APPEARANCE: BREAST CANCER PATIENT COHORT STUDY

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Purpose: Breast cancer patients experience various altered appearance throughout the treatments such as surgery, chemotherapy and radiotherapy. Altered appearance is one of the most common problems for breast cancer patients which is the contribute to the development of distress by affecting the patient's psychosocial impact such as body image, depression, daily activity, quality of life. However, altered appearance of distress has been associated with psychosocial impact, the longitudinal effect of altered appearance on distress and psychosocial impact in unknown. This study aimed to examine effect of altered appearance on distress and psychosocial impact during breast cancer over time.

Patients and Methods: Between July 2010 and May 2011, we recruited patients in the two cancer hospitals in Seoul 'Samsung Medical Center' and 'Seoul National University Hospital'. Women were recruited if they were primary diagnosis of breast cancer, with no execution of neo-adjuvant treatment (chemotherapy and radiation) prior to surgery, no evidence of metastasis or recurrence or current psychiatric disorder and who were less than 65 year age. Data were collected at 5 times points: enrollment (before surgery), post surgery (2 weeks post surgery), during chemotherapy (3 months post surgery), during radiotherapy (6 months post surgery) and 12 months post surgery. Trained oncology staffs assess altered appearance including weight change, body change, skin change, and hair loss. Study participants were asked to complete questionnaires on distress due to altered appearance, body image, anxiety, depression, quality of life, physical activities, fatigue, and menopause symptom at each visit. Total 435 breast cancer patients were initially contacted and accepted participated in the study. Of these, after excluding 8 patients with recurrence and 65 patients lost to follow-up, the present analysis is based on 411 patients.

Results: The mean age of the participants was 46.4 (SD 7.91) year old. 83.0% of participants were married, and 44.9% and 37.6% of them had stage I and II breast cancer, respectively. 83.0% of the patients had lumpectomy, and 70.6% and 85.9% had chemotherapy and radiotherapy, respectively. Altered appearance distress significantly increased over

time. Patients who received chemotherapy experienced almost double amount of distress compared to those without chemotherapy, and patients had the most distress during radiotherapy. Body image rapidly decreased at 3 month after surgery, and its effects lasted until 6 months after surgery. Patients who experience distress due to altered appearance were more likely to have lower quality of life and performed less physical activities. There were 21.9% and 43.5% had abnormal anxiety and depression before surgery respectively. The proportion of abnormal anxiety rapidly decreased after surgery ($p < 0.01$) while there was no significant change with depression. Patients who experienced altered appearance distress were more likely to have depression and lower quality of life.

Discussion: Breast cancer patients with altered appearance distress affecting patients' psychosocial impact throughout the treatment. Our findings contributed to the advance of suggested in this area, providing relevant data about the distress of altered appearance, it is associated with psychosocial impact among breast cancer patients. This study also suggested some clinical implications that can assist health professionals developing clinical pathways and education programs to help women with breast cancer manage altered appearance distress during active treatment.

Acknowledgement: The research was accomplished by the support from AMOREPACIFIC and Korea Breast Cancer Foundation.

SP11-2

IMPACT OF DAILY ACTIVITY AND PHYSICAL CONDITION ON QOL OF WOMEN RECEIVING CANCER CHEMOTHERAPY

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INTRODUCTION

Since the late 1960s, both mortality and morbidity of breast cancer have increased in Japan. According to the National Cancer Center (2005), one in 16 Japanese women will develop breast cancer at some time during their lives. However, the 5-year relative survival rate is higher than 80%, which is good in comparison with other cancers.

PHYSICAL ACTIVITY AFFECTS PATIENTS UNDERGOING CANCER TREATMENT

In Western countries, research indicates level of physical activity decreases significantly during and after treatment when compared with before the breast cancer was diagnosed, and sedentary lifestyle causes new health problems such as obesity (Irwin, 2003). Recent neuroscientific research has shown that proliferation of neural stem cells in the hippocampus is increased by exercise (Pereia, 2007). In humans, it was shown that memory is significantly improved and cell mass in the brain increased, when aerobic exercise of about 40 min/day was continued for months (Floel, 2010). Thus, maintaining physical activity may be a way to manage physical and cognitive function during cancer treatment.

IMPACT OF WALKING ABILITY AND PHYSICAL CONDITION ON FATIGUE AND ANXIETY

I previously reported the relationships among leg muscle strength (knee extension, ankle dorsiflexion and ankle plantar flexion) and step-count as walking ability, fatigue and anxiety in subjects who had undergone hematopoietic stem cell transplantation (HSCT) for hematological disease (Tonosaki, 2011). The results of a multiple regression analysis demonstrated that immediately before hospital discharge, which was an average of 120 days after transplantation, subjects with later recovery of adequate food intake after HSCT

and weaker knee extension strength per body mass reported higher fatigue. Knee extension strength per body mass was correlated with an average number of step-counts after transplantation, and fatigue was strongly correlated with anxiety. In addition, in a group whose body mass index (BMI) exceeded 23.5 kg/m2 before transplantation, stronger fatigue was related to the weaker of ankle dorsiflexion strength. Thus, physical inactivity causes decreased leg strength, which brings about a negative cycle of decreased walking ability. It is also related to anxiety. Moreover, decreased muscle endurance of the ankles, which have an important role in walking, occurred in people with a high body weight, making it difficult for them to walk at a fast pace for a long time. Subjects were examined at a mean time of 120 days after transplantation, which is similar to the duration of postoperative chemotherapy in breast cancer patients.

The average step-count for two months after discharge from the hospital in these same subjects who had higher step-counts reported stronger plantar flexion strength per body mass. People with BMI of < 22.0 kg/m^2 had significantly higher step counts than the others. The above indicates that muscle strength relates to walking ability by maintaining a high level of daily physical activity. If body weight is high, it is necessary to maintain muscle strength to oppose one's own weight.

STUDIES RELATED TO THE LEVEL OF PHYSICAL ACTIVITY, FATIGUE, AND HEALTH RELATED QOL (HRQOL) IN PATIENTS UNDERGOING CHEMOTHERAPY FOR BREAST CANCER

We are currently investigating the effects of the level of physical activity during breast cancer chemotherapy on fatigue and HRQOL in patients after surgery. Using a triaxial accelerometer (Panasonic Inc.), we measured the total time (min) of physical activity of ≥ 3 metabolic equivalents (Mets), total time (min) of physical activity < 3 Mets, number of step-counts, and energy consumption per day on each day of measurement. We also investigated the relationship between the physical activity and the health locus of control concept of controlling one's own health with one's internal control.

The aim of this study was to clarify the relationship between the level of physical activity and HRQOL in breast cancer survivors who are coping with the side effects of chemotherapy and readjusting to their daily life. These results provide basic data indicating that consciously maintaining an adequate physical activity is effective in the management of symptoms, so that treatment can be completed while high QOL is maintained. Moreover, we plan to investigate whether, in addition to assessing cognitive function, maintaining adequate level of physical activity can be a method of managing symptoms with regard to decreased cognitive function.

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FEMALE SEXUAL FUNCTION IN WOMEN WITH BREAST CANCER

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INTRODUCTION

Women with breast cancer suffer from long term problem with sexual functioning. Sexual problems that occur from cancer treatment do not tend to resolve within the first year or two of disease-free survival [1]. Sexual function including desire, excitement, orgasm, pain and satisfaction in women with cancer are widely affected by disease itself and its treatment [2]. Mastectomy, radiation therapy, chemo therapy and hormone therapy are the factors influencing sexual function in women with breast cancer [3]. As it is described in the category of Sexual Interest/Arousal Disorder in Women in DSM-V, psychosocial factors including women's generalized or situational factors, partner factors such as partner's sexual problems or health status, relationship factors such as poor communication, individual vulnerability factors such as poor body image, depression or anxiety, cultural/religious factors are the factors influencing sexual functioning in women with breast cancer as well [4].

PREVALENCE OF SEXUAL PROBLEM IN WOMEN WITH BREAST CANCER

Wide range of rates for the prevalence of sexual problems in breast cancer survivors has been reported. Among previous studies, 29% became asexual [5] and 70% reperted sexual problems [6] after breast cancer treatment. In one cohort study which investigated longitudinal changes in sexual problems in Korean cancer survivors, only 39%, 48%, 50% of women were sexually active at 3, 6, 12 month period respectively after treatment [7]. A recent study also suggested that among breast cancer group who had received chemotherapy or hormonal therapy in the prior six months, 50% had not had any sexual activity in the prior four weeks, and 40% had stopped having sexual intercourse at the beginning of their treatment [8]. A cohort study result indicated that 70% of Australian women with breast cancer within 12 months of their first diagnosis experienced sexual problems [6].

FACTORS AFFECTING SEXUAL FUNCTION IN WOMEN WITH BREAST CANCER

Women's sexual response can be affected in many ways, and the causes of sexual dysfunction are often both physical and psychosocial. Physical factors including age of women and partners, disease and treatment relating factors including physical distress, tumor stage, breast surgery, chemotherapy, adjuvant tamoxifen or aromatase inhibitor therapy, time after last treatment have been reported as primary factors influencing sexual function in women with cancer [2, 6, 9, 10]. However, physical changes after cancer treatment do not automatically lead to sexual problems or dysfunctions. Women's final sexual dysfunctions depend on their psychosocial factors as mediating variables. Psychosocial factors included body image, sexual attitude, sexual information, depression, and marital intimacy [2].

CONCLUSION

In conclusion, many women with breast cancer suffer from sexual dysfunction during and after treatment. Prevalence and affected factors of women's sexual dysfunction have been reviewed and discussed in this presentation. Well designed sexual program such as PLISSIT model program has been suggested to use in order to improve women's sexual function [11, 12].

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SP11-4

MOBILIXING SURVIVORS FOR ADVOCACY AND POLICY CHANGE

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We are a group of breast cancer survivors in Taiwan devoted to helping other women get rid of the challenges of breast cancer and delivering useful information for health care to reduce the harm caused by breast cancer. We hope that there are less and less women suffering the same pain like what we have gone through. With the mantra of "Care Women Care", we step out to voice significant issues in regard to breast cancer care and support as well as health. There is a Taiwanese song named "A little red flower growing on the stone" which depicts a little red flower still erects glamorously and beautifully even if the growing environment is difficult. A little red flower is just like breast cancer survivors who have weathered the life-threatening disease and have continuously empowered themselves to be able to make differences in their lives and achieve a more meaningful life. Breast cancer is the leading cause of cancer incidence among women in Taiwan. According to the figures announced by Taiwan Government, there are 8,136 new cases diagnosed and 1,654 people died from breast cancer in 2008. One in 19 women in Taiwan would probably be diagnosed with breast cancer in their lives. Moreover, the breast cancer incidence rate per 100,000 in Taiwan is 48 based on a medical survey report, which accounts for the threat from breast cancer which is tremendous to the lives of Taiwan women. Reach to recovery Program was introduced into Taiwan in 1990s, which inspired hospitals to found breast cancer support group in succession. Taiwan Breast Cancer Alliance (TBCA) originated from an annual reunion of breast cancer groups of Taiwan, and was officially chartered in 2002 as a nationwide breast cancer support group. It is now has 37 group members and more than 15,000 individual members. Whenever mentioning "Advocacy", people would associate it with politics. In fact, it is an instrument used for drawing the attention of the public and government on issues or policies needed improving, which aims to influence public-policy, research agendas, and resource allocation. Since 2005, TBCA has advanced studies to explore the needs and interests of breast cancer patients and survivors, and then convert the results of studies into feasible programs. The details of the studies and programs derived from will be introduced by years during the presentation. In addition, two successful cases from TBCA will be shared at the symposium, 1) Successfully lobbying for Taiwan Government to

add Herceptin to its list of preferred treatments for early breast cancer patients, 2) Walking all over the whole Taiwan Island, totaling 369 townships, within 3 years (starting from 2009) for promoting breast cancer awareness. The life cycle could be staged into birth, illness, aging and death. No one is able to bypass any of them. People can not live without medical care and support services which requiring our continuous investment to make them better and better. The bell for the 16th RRI Breast Cancer Support Conference is ringing. From 9 to 12 November 2011 in Taipei, please come to join us to explore more about the breast cancer support and reach towards a new Horizon for our lives and cancer care.

SP12-1

INTRODUCTION OF TEAM SCIENCE IN TREATMENT OF BREAST CANCER IN FUDAN UNIVERSITY SHANGHAI CANCER CENTER

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Founded in 1931, Fudan University Shanghai Cancer Center is the oldest and one of the largest cancer centers in China. It is a high volume hospital with 12 multidisciplinary management teams (MDT) for different tumors. Among them, the MDT team for breast cancer is the best and most productive team which treats nearly one quarter to one third of patients in our center and published the most papers in international journals. Our success results from following reasons: 1) A good reputation which has been established by old generation of experts; 2) A strong head which is good at surgery and experiment as well as leadership; 3) a free academic atmosphere which gives full play of staff's talents; 4) nice cooperations between Departments, and between bench and bedside. We have a lot of activities to provide good training foryoung staff and to promote the cooperations. For example, all clinical doctors, radiologists, pathologists, research nurses, young fellows and so onare required to take part in the MDT outpatient clinic, which lasts one hour every Wednesday morning. The one hour real patient-based discussion usually deals with patients difficult to diagnose or to treat, or those with rare breast disease.

CLINICAL TRIAL

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Clinical trials are studies involving people that help to make progress in preventing, diagnosing, and treating cancer. Improvements in cancer treatment based on results of cancer clinical trials have led to improved clinical outcomes with survival advantages in patients with cancer. Despite the promise offered by clinical trials, less than 5% of cancer patients enroll in clinical trials. This lack of participation slows progress in the development of new, more effective therapies. Moreover, clinical trials may requires hundreds or even thousands of people and it often takes a long time to find out the results. The need for global collaboration on clinical trials has correspondingly increased. Global collaborations will result in maximization of our resources and patients, permitting us to complete clinically important trials in a timely manner. Integration of investigators and cooperative groups in Asia-Pacific regions as well as others in Western countries and well-organization of clinical trials networks will make our clinical trials more efficient and representative of cancer patients from around the world and the results from our clinical trials will be more globally applicable to those patients. Recent advances in molecular biology have allowed us the use of molecular biomarkers to define patient cohorts based on tumor biology. Some "smart" cancers have multiple simultaneous mutations with large mutational load and may require the targeting of multiple drivers. "Magic shotgun" will be needed for these tumors aiming at multiple targets in multiple pathways. In addition, molecular heterogeneity of human cancer both between patients with one type of cancer as well as between tumor cells within one patient exist, population-based unselected approaches have major limitations for the development of novel cancer therapeutics. Current clinical trials system in cancer largely involve a traditional evidence-based, population-based, unselected approach that focuses on treating patient populations with molecularly uncharacterized disease and is not designed to handle genomic chaos with multiple drivers as well. We need a vibrant clinical trial system as well as international collaboration system that will bring us to better care for our cancer patients in the era of genome-driven therapy.

SP12-3

BRIDGING CANCER RESEARCH OPPORTUNITY BETWEEN US AND ASIA

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With the application of molecular biology in oncology research, there is a recent rapid expansion of novel drugs in research and development (R&D) globally. However, majority of the new drug development was traditionally from the industrialized countries such as United States where most of pharmaceutical companies were based and where there were ample new molecules and funding for preclinical and clinical studies. However, lack of patient population and complicated protocol approval mechanism were limiting factors for many new drugs R&D in USA in the past. This has led to recent major restructuring of cooperative groups in USA in a hope to increase the efficiency and decrease the cost of clinical research. Many pharmas are now looking to developing countries to conduct R&D although some developing countries lack the infrastructure and standard of care for preclinical and clinical research that meet FDA requirement. In addition, some developing countries have local policies on new drug including investigational drugs approval that is lengthy, which further delay the availability of new drugs in these countries. Finally, the education gap between the industrialized and developing countries is still a limiting factor in the appropriate utilization of new drugs in cancer patients.

USCACA was formed to bridge the gap between the USA and China in cancer drug R&D. It is a not-for-profit organization to promote collaborations in cancer research, treatment, education and prevention between US and China with over 750 Members from academia, industry, and regulatory agencies in USA and China. It broadly collaborates with associations and organizations dedicated to cancer research, treatment and prevention such as ASCO and AACR in USA and CACA and CSCO in China. Fostering collaborations among different countries and organization helps to offer efficient drug development with safety and efficiency which ultimately benefits cancer patients globally.

SP12-4

DEVELOPMENT OF MANPOWER AND HUMAN RESOURCES IN BREAST CANCER RESEARCH AND MANAGEMENT: JAPAN

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In order to develop novel therapeutics and diagnostics, team science is indispensible. Especially the formation of international collaborative team is a key issue to realize a good success. In a variety of situations such as clinical trials, translational research and informatics, academic network as well as human resources enables us to make something fruitfully. In recent days, these activities increased remarkably in Japan. In addition, interdisciplinary collaboration with engineering and computer science has been also activated. We need to have a team with different knowledge, skills and ideas. Encouragement of exchange investigators and students should be more accelerated.

SP13-1

CHRONOLOGICAL CHANGES OF CLINICAL CHARACTERISTICS OF KOREAN BREAST CANCER PATIENTS DURING 14 YEARS (1996-2010) USING ON-LINE REGISTRATION PROGRAM

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INTRODUCTION

Breast cancer is the second most frequent cancer among Korean women. The increased incidence is attributed to a westernized lifestyle. Patients and Methods The Korean Breast Cancer Society (KBCS) started a nationwide multicenter survey in 1996 with a paper questionnaire. Since 2001, it has progressed to the on-line registration system. We collected data from newly diagnosed primary breast cancer patients recruited at 35 universities (57 surgical training hospitals), 23 general hospitals, and 6 private hospitals in 2010, and analyzed the chronological changes in several clinico-pathologic factors and risk factors.

SUMMARY

This report shows the following several outliers:

- Increase in the number of patients and incidence rate. ? Increase in the rates of detection with screening
- High proportion of premenopausal patients
- Increase in the proportion of breast-conserving operations and immediate reconstruction after mastectomy
- Increase in the percentage of early breast cancer
- Increase in patients with some risk factors
- Increased survival rate in most stages

CONCLUSIONS

Our results suggest that the clinical characteristics of Korean breast cancer patients are following the patterns of Western countries, and the incidence of breast cancer in Korea

will continue to rise. We need to understand the characteristics of breast cancer among Koreans, and how this differs from other countries, through continuous investigations as on-line registration systems in the future.

SP13-2

THE TREND OF BREAST CANCER DIAGNOSIS AND TREATMENT DEDUCED FROM BREAST CANCER REGISTRATION IN JAPAN

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Background: The aim of tumor registration is to register patients diagnosed with breast cancer and to get information relevant to their diagnosis (such as stage, hormone receptor status, etc.), treatment (surgery, radiation, chemotherapy, hormone therapy, etc.), and survivorship. This data includes relevant demographic information such as age, menopausal status, body mass index (BMI), and place of residence. In Japan, the new system of registration began in 2005 using the internet. In this study, the patient's characteristics and treatments were analyzed to identify possible trends. Patients and

Methods: The breast cancer registration that began in 1975 collected 188,265 cases every 29 years until 2003, and they were all registered using the old system. Under the new system, 14,805 cases were registered in 2004, 19,509 cases in 2005, 20,510 cases in 2006, 23,633 cases in 2007, 30,440 cases in 2008, and 33,834 cases in 2009. In a relatively short period of time the number of breast cancer cases has increased, and as a result the number of registered institutions has increased to 576. In this study, we compared the data in 2009 with the data in 2004.

Results: 1) Patient background: The median age was 56 years in 2004 and 58 years in 2009, and postmenopausal patients were 62.6% in 2004 and 63.8% in 2009. The rate of patients detected by mass screening increased from 20.4% to 30.1% in 2009. The BMI of the patients remained consistent in two-thirds of patients who were categorized as the healthy weight group. 2) Tumor characteristics: Tumor size of < 2.0 cm and stage classification of < stage I were 44.9% and 40.1% in 2004 and increased to 54.3% and 50.7% in 2009, respectively. Patients with node negative were 58.7% in 2004 and 67.2% in 2009. Moreover, the rate of non-invasive carcinoma was 8.5% in 2004 and 15.3% in 2009. This means that more patients can be detected for early stage tumors than in the past. 3) Surgery: The rate of breast conserving surgery (BCS) was 50.1% in 2004 and increased to 59.5% in 2009. Sentinel node biopsy was performed in 18.3% in 2004 and 51.8% in 2009. This does not include the patients with axillary dissection after positive sentinel nodes.

Radiotherapy after breast conserving surgery was performed in 72.3% of the cases in 2004 to 81.0% in 2009. There were more cases involving less invasive surgery with radiotherapy in 2009. 4) Biological marker-subtype: There were significant differences of positive rates in ER, PgR and HER2 (marginal) between the 2 groups. The positive rates increased to 75.2%, 62.3% and 14.9% in 2009 from 71.8%, 58.8%, and 12.4% in 2004. The distribution of subtypes in 2009 were as follows; HR+HER2- in 71.4%, HR+HER2+ in 8.2%, HR-HER2+ in 8.2% and HR-HER2- in 12.3%. 5) Treatment: Preoperative therapy was performed in about 10% of the cases, whereas postoperative therapy was performed in about 80% of the cases. Regarding treatment regimen, patients who were treated with taxane and aromatses inhibitor (AI) increased in 2009. Moreover, trastuzumab was used more often in 2009. Thus, the numbers of registered cases and institutions increased. Moreover, there were more cases with smaller tumors, node negative, less invasive surgery (BCS and SLNB), and treatment using taxane and AI. The surgical operation and treatment information data base project known as the National Clinical Database (NCD) began this year. Data to be registered includes surgical information and type of treatment performed at each facility. The JBCS will be connected to this system next year.

Conclusion: A significant trend in breast cancer diagnosis and treatment was identified by using the new registration system in Japan, that collects valuable information that has contributed to improvements at the treatment and diagnostic level.

SP13-3

THE ROLES OF NATIONAL CANCER REGISTRY: EXPERIENCE OF THE CHINA

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Cancer registries are urgently needed in developing countries, including in China. However, there was only two cancer registries stations in whole country in early 1960's. Registry work has developed rapidly since 1990's. The Chinese cancer registration system covered 40.81 millions of population (3.3% of the whole population of China) in 2000. In 2002, National Central Cancer Registry was established. Up to October 2002, twenty of 31 provinces in the mainland of China had developed the cancer registration, it covered with 75.27 million population (5.96% of the whole population). In 2010, Fiscal transfer payment Program from central government (11.50 millions Yuan, 193 cancer registries) covered 13% of the whole population of China. Numbers of cancer registries were increased from 2 in 1960 to 193 in 2010. Currently, the international classification of disease has been applied to disease classification in all cancer registration stations. Certainly, national cancer registries can help us to know the cancer burden and the extent of the cancer so that programmes for cancer control can be planned efficiently, to implement standards of care and define prevention strategies.

GBCC2011

Closing Lecture

THE CHALLENGE OF ATTRACTING MEDIA ATTENTION TO BREAST CANCER ADVOCACY

Noreen Fraser

President and CEO, Noreen Fraser Foundation, USA

As a woman, living with metastatic breast cancer for 10 years, I will describe the process by which I went from patient to advocate, and how that eventually led to my co-producing Stand Up To Cancer, a network television special that raised 100 million for cancer research. The statistics are staggering. In 2010, 1.5 million people heard the words, "you have breast cancer." In the United States alone there are 527 new cases of breast cancer per day and 110 deaths per day. Prediagnosis, most global citizens are unaware of these staggering statistics. To them, cancer is a pink t-shirt , a group walk, or an annual donation. I was one of those people.

I will talk about the process of researching and learning why the "cure" looked truly unattainable to me. It was not until I understood that the business of cancer promotes competition and not collaboration, that I knew I had to become an advocate. I also had discovered that the research money was divided up amongst too many projects. There needed to be larger investments funnelled into a few of the most promising projects and into translational research which will get effective therapies to patients more quickly. The question I had to ask myself was what could I do as an individual to create an awareness of the flaws in the status quo? It was then that I realized that my background as a television producer was the vehicle to promote this idea. The next step was a collaboration with colleagues in my field to create a network television show. The show would have to promote change. It would have to offer a new approach to a broken system which would be compelling enough to convince people to donate money. And it would have to have celebrities to bring in the viewers.

I will talk about the difference between raising money and media awareness when you have three networks behind you and raising money as a start up foundation which I have done with the Noreen Fraser Foundation. I will show how my idea of engaging men (Men For Women Now) to be advocates for the women they love has increased awareness for early detection. I have learned that laughter is a universal language as well as a healer. By having comedians do funny viral videos, we have reached a younger audience. Un-

derstanding the importance of early detection and passing it on to your loved ones will save lives.

Not everyone has access to celebrities. You can garner media attention by following the steps I will provide. Whether your advocacy group is local or national there are always ways to create media interest.

CL2

PSYCHOSOCIAL ASPECT OF BREAST CANCER RISK

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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 examine the relation of stress to breast cancer risk. First, we will overview classic theory of 'fight or flight' response to stress. Second, we will present two possible mechanisms how stress may trigger the onset of breast cancer such as biological mechanism and behavioral mechanism. Finally, we will present the results of epidemiological studies focused on biologic basis for research on the role of stress in breast cancer incidence. Despite of plausible biologic mechanisms, it has not been well established the relationship between psychosocial factors and breast cancer risk. The most extensively studied psychosocial factors in relation to breast cancer incidence are stress and stressful life events. While some studies have found an association of stress with breast cancer, several other studies have reported no relationship between stress and breast cancer risk. With these mixed results, alternate model was proposed to consider the importance of understanding and modeling interactions between the factors (i.e., psychological stress and social supports) in relations to breast cancer risk. More research is needed to consider other factors such as genotype, social environment (e.g., SES), and individual characteristics in coping and personality. We suggest that increasing our understanding of the association of stress with breast cancer will require a transdisciplinary approach that includes research scientists from field of anthropology, psychology, sociology, genetics, molecular biology, epidemiology, and biostatistics.

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FP1-1

THE RISK OF BREAST CANCER ASSOCIATED WITH SPECIFIC MUTATION OF BRCA1 AND BRCA2 AMONG KOREAN POPULATION

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Background/Purpose: Carriers of germ-line mutations in BRCA1 and BRCA2 were at high risk for breast cancer. However, the risks were vary according to method for estimation method and penetrance of BRCA1/2 mutation was not estimated in Korean population.

Methods: We used Korean Hereditary Breast Cancer Study (KOHBRA) data. Blood samples and pedigree data from familiar or high-risk breast cancer patients were collected and BRCA1/2 status were identified with blood test. We estimated the risks of breast cancer through using genotyped proband design by comparing the cancer histories of first degree relatives of carriers of the mutations and noncarriers.

Results: 2022 breast cancer patients with BRCA1 or BRCA2 mutation and 9772 first degree relatives of the probands were identified. By the age of 80, the estimated risk of breast cancer among total BRCA1/2, BRCA1 and BRCA2 carriers were 17.8%, 23.8% and 13.7%, respectively. Among female, the estimated risks were 33.8% for BRCA1/2 carriers, 44.9% for BRCA1 carriers and 26.7% for BRCA2 carriers. Among total noncarriers, the estimated risk of breast cancer was 8.8% by the age of 80 and 16.3% among female noncarriers.

Conclusion: The risks of breast cancer were higher among BRCA1/2 carriers than noncarriers. The risk among noncarriers may be overestimated because they are the relatives of breast cancer patients. Although limitations, this study is the first study estimating penetrance of BRCA1/2 mutation in large number of population.

Free Paper

FP1-3

METFORMIN INHIBITS THE GROWTH OF HUMAN BREAST CARCINOMA (MCF-7) MAMMOSPHERE CELLS PROMOTED BY ESTROGEN, TCDD, AND BIS-PHENOL A

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Background/Purpose: Metformin, a Type II diabetic treatment drug, inhibits transcription of gluconeogenesis genes, has been shown to lower the risk of some diabetes-related tumors, including breast cancer. Recently, "cancer stem cells" have been shown to that sustain the growth of tumors and are resistant to therapy.

Methods: To test the hypothesis that metformin might be reducing the risk to breast cancers, the human breast carcinoma cell line, MCF-7, grown in 3-dimensional mammospheres, were treated with various known and suspected breast cancer chemicals (estrogen, 2,3,7,8-tetrachlorodibenzeodioxin (TCDD), and endocrine-disruptors, bis-phenol A, phenol red), with and without non-cytotoxic concentrations of metformin. Using Oct4 expression as a marker for the cancer stem cells, the number, size and were measured in these cells.

Results: Results demonstrated that TCDD (100 nM) and Bis-phenol A (10 μM) stimulated the number of mammospheres and size of the mammospheres, as did estrogen (10 nM E2). By monitoring a cancer stem cell marker, Oct4, the stimulation by these chemicals was correlated with the increased expression of Oct4. On the other hand, metaformin at 1 and 10 mM concentration dramatically reduced the size and number of mammospheres.

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gen (10 nM E2). By monitoring a cancer stem cell marker, Oct4, the stimulation by these chemicals was correlated with the increased expression of Oct4. On the other hand, metaformin at 1 and 10 mM concentration dramatically reduced the size and number of mammospheres.

FP1-4

PREDICTIVE FACTOR OF UNDERESTIMATION OF ULTRASOUND-GUIDED CORE NEEDLE BIOPOSY (cnb)

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Background/Purpose: Predicting the risk of underestimation after ultrasound-guided core needle biopsy (CNB) is crucial when making surgical decision of atypical ductal hyperplasia (ADH) or ductal carcinoma *in situ* (DCIS) whether to perform oncologic surgery or excisional biopsy. Stratification of predictive factors associated with underestimation and validation of previously suggested scoring system was done.

Methods: We retrospectively reviewed 85 ADH patients undergone sequential surgical excision between Feb 2007 and Feb 2011 and 506 DCIS patients between Jan 2000 to Feb 2011. The clinicopathologic factors associated with upstaging to 'malignancy from ADH' and 'invasive cancer from DCIS' was evaluated and scoring system from EY Go et al. was validated.

Results: In ADH, underestimation rate was 36.5% (31/85). 4.7% (4/85) had invasive foci and 31.8% (27/85) had *in situ* carcinoma. In univariate analysis palpability, microcalcification, size showed significant association with underestimation ($p < 0.001$, $p = 0.028$, $p < 0.001$). The validation score showed significancy ($p < 0.001$, ROC curve AUC 0.818). In multivariate analysis palpable, microcalcification (+), age ≥ 50 years showed significancy (OR 17.88 $p < 0.001$, OR 5.93 $p = 0.015$, OR 4.05 $p = 0.037$). In DCIS, underestimation rate was 42.7% (216/506). Palpable, bigger size, mass in MMG, higher BI-RADS, 14-gauge, higher grade showed significancy in univariate analysis (all $p < 0.001$). In multivariate analysis palpable, bigger size, high grade, 14-gauge had association (OR 1.89 $p = 0.005$, OR 1.02 $p = 0.002$, OR 1.71 $p = .015$, OR 1.69 $p = 0.026$). 20 (4.91%, 20/407) were lymph node (+) and size ≥ 20 mm was independently associated with positivity (OR 3.42 $p = 0.038$).

Conclusion: Underestimation is more likely in age ≥ 50 years, palpable, microcalcification (+) ADH and achieving adequate margin should be considered. Making plans of surgery in palpable, high grade, bigger size, 14 gauge CNB diagnosed DCIS, risk of upstaging should be regarded.

FP2-1

CLINICOPATHOLOGIC CHARACTERISTICS OF BREAST CANCERS DETECTED BY ULTRASOUND

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Background/Purpose: Screening ultrasound (US) can increase the detection of breast cancer. However, little is known about the clinicopathologic characteristics of breast cancers detected by screening US.

Methods: During a 7-year period, a total of 6,837 women underwent surgery for breast cancer at our hospital. Of 6,837 women, 1,047 were asymptomatic and had a non-palpable cancer. Two hundred fifty-four women with 256 cancers detected by US (US-detected cancer) and 793 women with 807 cancers detected by mammography (MG-detected cancer) were identified. The imaging, clinicopathologic and molecular data were reviewed. Univariate and multivariate analyses were performed.

Results: Women with US-detected cancer were younger and were more likely to undergo a breast-conserving surgery and to have node-negative invasive cancer ($p < 0.0001$). By multivariate analysis, the significant independent characteristics were the tumor size, molecular subtype, PR, HER2, mammographic density, and final BI-RADS assessment category. Compared to tumors that were > 2 cm in size, tumors that were ≤ 1 cm in size were 2.2 times more likely to be US-detected cancers ($p = 0.02$). Compared to the luminal A subtype tumors (ER+, PR+, HER2-), luminal B subtype tumors (ER+, PR+, HER2+) were less likely to be in the US-detected cancer group ($p < 0.01$). Women with dense breasts were more likely to have US-detected cancer ($p < 0.01$) versus those with non-dense breasts. US-detected cancers were less likely to be diagnosed as category 5 instead of category 4 ($p < 0.01$).

Conclusion: Women with US-detected breast cancer are more likely to have small-sized invasive cancer and more likely associated with the luminal A subtype.

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FP2-2

LYMPHOVASCULAR INVASION AND TUMOR SIZE ARE PREDICTORS OF SENTINEL LYMPH NODE INVOLVEMENT IN CLINICALLY NODE NEGATIVE BREAST CANCER PATIENT

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Background/Purpose: Nodal status in breast cancer patients remains one of the most important prognostic factors. The purpose of this study is to evaluate predictors of sentinel lymph node (SLN) involvement.

Methods: A retrospective review of all clinically node negative breast cancer patients who underwent SLN biopsy with or without axillary node dissection (AND) between April 2008 & July 2010 in our tertiary care center.

Results: A total of 117 patients (invasive ductal carcinoma 111, invasive lobular carcinoma 6) were included in the study. Forty patients (34.2%) had T1 tumors, sixty two (53.0%) had T2 tumors, seven (6.0%) had T3 tumors, and eight (6.8%) had unknown T size. The SLN was identified in 107 out 117 patients (91.5%). The number of SLN removed ranged from 1-10 nodes with a mean of 2 nodes. The SLN was positive in 39 patients (36.4%). 37 patients with positive SLN underwent AND with a mean of 15.8 lymph nodes dissected. Additional positive nodes were found in 15 patients (40.5%) with a mean of six positive nodes. Multivariate analysis revealed that the only significant variables that predicted SLN involvement were lymphovascular invasion (LVI), T2 tumors size, and T3 tumor size with a p value of 0.001, 0.030 and 0.013, respectively. Tumor biology, histological grade and multifocality were not significant predictors of SLN involvement. No significant predictors of non-sentinel lymph node (non-SLN) involvement were found.

Conclusion: LVI and tumor size (T2 and T3) are significant predictors of SLN involvement in clinically node negative breast cancer patients.

FP2-3

EVALUATION OF TUMOR SIZE IN BREAST CANCER PATIENTS USING MRI NAVIGATED ULTRASOUND (US)

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Background/Purpose: This study was to evaluate the accuracy of magnetic resonance imaging (MRI) navigated US in comparison with US without MRI navigation for tumor size measurement.

Methods: Between October and December 2010, 53 patients (mean age, 51.9 years; range, 24-65 years) with 60 breast cancers (mean size, 2.8 cm; range, 0-88 cm) underwent breast MRI and US with or without MRI navigation (volume navigation, logiq E9, GE) for surgical planning to surgical excision. Maximum lesion size at initial breast US without MRI navigation and preoperative MRI-navigated US were measured and their correlation with pathologic measurements were assessed using Pearson's correlation. Absolute discrepancies between MRI-navigated US measured tumor size and pathologic tumor size were compared between subgroups defined by various clinicopathologic profiles of the patients.

Results: There were 53 invasive ductal carcinomas with or without ductal carcinoma *in situ* (DCIS), 5 pure DCIS, 1 invasive lobular carcinoma, and 1 metaplastic carcinoma. Neoadjuvant chemotherapy was performed in 17 patients. Mean lesion size at breast US without MRI navigation and at MRI-navigated US was 1.9 cm and 2.4cm, compared with 2.8 cm on the pathology. Pearson's correlation of the size measured at US without navigation and pathology was 0.540 versus 0.688 for MRI-navigated US and pathology ($p < 0.001$). Minimal discrepancy between MRI-navigated US tumor size and pathology was noted in patients who received neoadjuvant chemotherapy, did not have DCIS component, whose tumor was less than 5cm, and was of mass type on MRI.

Conclusion: MRI-navigated US was more accurate for tumor size estimation than breast US without MRI navigation.

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FP2-4

BILATERAL PREOPERATIVE MR EXAMINATIONS IN NEWLY DIAGNOSED BREAST CANCER PATIENTS: INITIAL AND LONG-TERM IMPACT ON CONTRALATERAL BREAST CANCER DIAGNOSIS

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Background/Purpose: We assessed whether bilateral preoperative MRI could reduce contralateral breast recurrence at long term follow-up.

Methods: In 2007, bilateral breast MRI replaced unilateral breast MRI in our institution. We compared the cancer detection rates of 1771 consecutive bilateral breast MRI and 1323 unilateral breast MRI for women with newly diagnosed breast cancers. There were no significant differences in mean patient age and stage between the two groups. Median FU duration was 56 months (range: 13-86 months) for the unilateral scan group and 32 months (range: 12-51months) for the bilateral scan group.

Results: At the time of preoperative evaluation, contralateral cancers detected by mammography and physical examination were similar between the two groups [2.1% (38 of 1771) vs. 1.3% (18 of 1323), p = .13]. However, 25 additional cancers were detected by MRI in the bilateral scan group compared to the unilateral scan group, [1.4% (25 of 1771) vs. 0% (0 of 1323), p = .0001]. Long-term FU revealed that the number of contralateral breast cancer diagnoses in unilateral scan group was greater than that in the bilateral scan group [2.2% (29 of 1323) vs. 0.8% (14 of 1771), p = .002]. Median interval between initial cancer surgery and contralateral cancer diagnosis was 44 months (range: 8-76 months) in the unilateral scan group and 32 months (range: 7-48 months) in the bilateral scan group.

Conclusion: Introduction of bilateral MRI to preoperative evaluation in breast cancer patients increases contralateral breast cancer detection, potentially leading to the reduction of contralateral breast cancer recurrence at long-term follow-up.

FP2-5

MULTIPLE MARGIN POSITIVITY IN FROZEN SECTION AS A TRIGGER FACTOR TO LOCAL FAILURE OF BREAST CANCER SURGERY

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Background/Purpose: Margin status after breast conserving surgery impacts on local control and intra-operative remnant tissue frozen section reduces margin positive rates. Although the negative result of margin status improves local control, multiple or extensive margin positive which are shown in more than twice times or 2 different sites triggers local failure. Authors performed this study to evaluate the relationship between local recurrence and multiple margin positivity in total-circumference intra-operative frozen section.

Methods: A total of 410 patients who undergone breast conserving surgery between 1999 and 2003 were evaluated with 10-year disease free survival (DFS). Intra-operative frozen sections were obtained from breast remnant parenchyma (which is further from cancer) in each of clockwise directions. Margin positive cases were defined as those including atypia or carcinoma cells in frozen sections and immediate re-excision was performed when the positive margin was diagnosed.

Results: The local control rate at 10 years was 93.41% (383 cases). Final margin positive result was confirmed in 11 cases (2.68%) which were not reported on frozen section and 4 invasive cases were performed re-operation. Among 83 cases of margin positive on intra-operative frozen, multiple margin positive result cases were 38 cases (9.27%). 10-yr DFS rates were significantly worse on final margin positive cases ($p < 0.0001$) or multiple margin positive cases ($p = 0.0005$).

Conclusion: Margin positive case on final pathology is needed re-excision. And multiple margin positive case also would be an indication of wider excision or nipple-sparing mastectomy, if necessary.

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FP3-1

MANAGEMENT OF EARLY BREAST CANCER: PATTERNS OF PRACTICE IN PAKISTAN

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Background/Purpose: Breast cancer (BC) is a significant public health problem in Pakistan, a low to middle-income country (LMC) with the second highest incidence of BC in Asia. Clinical practice guidelines developed internationally for LMCs, aim to improve breast healthcare according to available resources. Applicability of such recommendations in Pakistan can be assessed by looking at current practice in breast cancer management. The current study describes the management of early BC and factors associated with surgical procedure conducted between 2002-2006 at one institute in Pakistan.

Methods: Data on 687 BC cases, diagnosed between 2002-06 were obtained from Department of Surgery-Aga Khan University Hospital, Karachi, Pakistan. Tumours with Stage I&II cancer were considered early BC. Final analysis was conducted on 325 early BC cases. Data were analysed using descriptive statistics and logistic regression analysis to examine associations of personal, demographic and tumour characteristics with surgical procedure.

Results: Breast Conservation Surgery (BCS) was conducted for 36% cases while post BCS 79.3% women received adjuvant radiation therapy. Multivariate analysis demonstrated that women with Stage I cancer (aOR: 5.4; 95%CI: 2.6-11.2) and single (aOR: 5.8; 95%CI: 1.2-28.7) were significantly more likely to receive BCS adjusting for age, history of hormone use, histologic grade and position of tumour.

Conclusion: Fewer women with early BC are receiving BCS than mastectomy and not all receive post BCS radiation therapy. These findings suggest that although BC treatment in Pakistan is in conformity with some recommendations of guidelines developed for LMCs, there is considerable room for improvement.

FP3-2

C-MET EXPRESSION AND MOLECULAR TARGETING THERAPY IN TRIPLE-NEGATIVE BREAST CANCER

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Background/Purpose: Triple-negative breast cancer (TNBC), which is characterized by negativity for ER, PR, and HER2, is a high risk breast cancer that lacks specific targets for treatment selection. Reportedly, the prognosis of breast cancer is correlated with HGF/c-met coexpression and c-met overexpression. c-met signaling plays an important role in the proliferation of breast cancer cells. However, few reports have been published regarding their correlation with TNBC. Here, we examined the correlation between TNBC and c-met expression and the effects of c-met inhibitors in TNBC cell lines.

Methods: A total of 1,036 patients who had undergone resection of a primary breast cancer at our institute were enrolled. ER/PR/HER2 status and c-met expression were assessed by immunohistochemistry. In vitro study, TNBC cell lines, MDA-MB 231 and OCUB-2, and non-TNBC cell lines, MCF-7 and OCUB-1, were used. c-met mRNA expression was examined by RT-PCR. Then, the effects of HGF, c-met siRNA, and c-met inhibitors on the proliferation of breast cancer cell lines were examined.

Results: The 1,036 patients included 190 TNBC patients, whose prognoses were poorer than those of non-TNBC patients. In the TNBC patients, the c-met gene expression-positive group showed a poorer prognosis than the control group. c-met was expressed in the TNBC cell lines, whose proliferation was enhanced by HGF. c-met kinase inhibitors and c-met siRNA inhibited the proliferation of TNBC cell lines.

Conclusion: c-met expression is a potential molecular target and useful in classifying TNBC.

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FP3-3

YOUNG AGE IS ASSOCIATED WITH IPSILATERAL BREAST TUMOR RECURRENCE AFTER BREAST CONSERVING SURGERY AND RADIATION THERAPY IN HER2-POSITIVE/ER-NEGATIVE SUBTYPE

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Background/Purpose: It has been known that younger patients had higher rate of ipsilateral breast tumor recurrence (IBTR) after breast conserving surgery (BCS). However, the biology under this relationship has not been elucidated. We investigated whether young age is associated with high IBTR in a certain subtype of breast cancer.

Methods: We analyzed data of 2,102 consecutive breast cancer patients who underwent BCS in two institutions of Korea between 2000 and 2005. Patients were classified into younger age group (≤ 40; YA) and older age group (> 40; OA). Breast cancer subtype was determined by estrogen receptor, progesterone receptor, and HER2 expression. All patients received radiation therapy (RT) after surgery. No patient received adjuvant trastuzumab.

Results: 513 patients were in YA and 1,589 were in OA. Median follow up duration was 61 months. The 5 year IBTR rate was 3.4% in YA compared to 1.1% in OA ($p < 0.001$). Subtype analysis showed that IBTR rate of YA was significantly higher than that of OA in luminal A and HER2 subtype ($p = 0.015$ and $p < 0.001$, respectively). Multivariate analysis with luminal A subtype in OA as reference showed that HER2 subtype in YA was associated with increased IBTR (hazard ratio = 12.24; 95% CI, 2.54-57.96). In OA, HER2 subtype was not associated with increased IBTR.

Conclusion: Young age women (≤ 40) had higher IBTR rate after BCS and RT than older women. This difference in IBTR could be seen mainly in HER2 subtype. Aggressive local control and adjuvant therapy should be considered for the young women with HER2 subtype tumor.

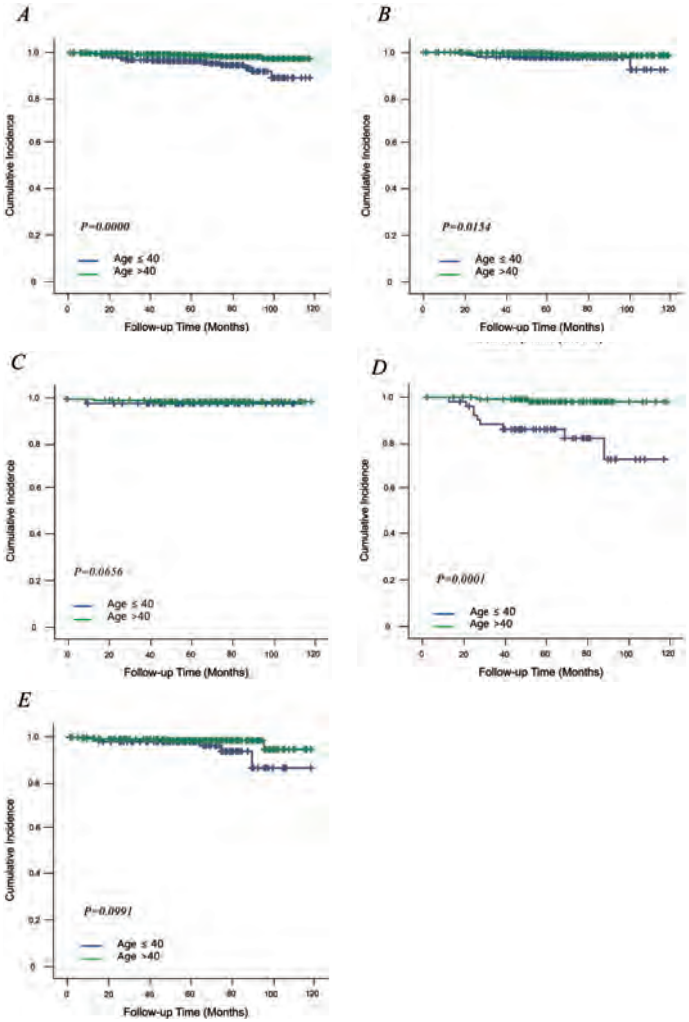

Fig. 1

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FP3-4

THE NUMBER OF SENTINEL LYMPH NODES REMOVED AND QUALITY OF LIFE AMONG EARLY BREAST CANCER PATIENTS DURING ACTIVE TREATMENT

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Background/Purpose: Sentinel lymph node biopsy (SLNB) has become an alternative procedure of axillary lymph node dissection with a lower risk of significant operative morbidity. However, few studies reviewed the relationship between the number of lymph nodes (LN) and morbidity. The aim of study was to evaluate whether the number of LN removed and quality of life after SLNB.

Methods: From Jun-2010 to April-2011, patients treated with SLNB were enrolled from two cancer hospitals in Korea. Data were collected preoperatively and at 2 weeks, 3 months, and 6 months after operation. Quality of life was assessed by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30 and BR23 and clinical data were obtained through medical records.

Results: Total 258 women with breast cancer participated in the study. There were 91, 112, and 55 patients who had 1 to 3, 4 to 6, and 7 or more lymph nodes removed respectively. While there was no statistical difference with body image, pain, breast symptom, and arm symptom between patents who had 1 to 3 LN removed and patients who had 4 to 6 LN removed, patients who had 7 or more LN removed reported lower body image and more breast symptom at 3 months after surgery. Details of quality of life and its pattern of change were in Table 1.

Conclusion: Number of lymph nodes removed during the surgery was not associated with quality of life among breast cancer patients. Therefore, SLNB was enough for the biopsy and may also lower the cost of the procedure and reduce morbidity.

Table Number of sentinel lymph nodes removed and quality of life

Variable	SLNs 1-3 N (%)=91 (35.3)		SLNs 4-6 N (%)=112 (43.4)		P-value	SLNs6 N (%)= 55 (21.3)		P-value
Body image (range 0-100)								
Mean (SD) at baseline	81.3 (19.45)		81.3 (21.16)			78.3 (21.33)		0.65
Change from baseline to 2 weeks (95% CI)	-8.05	(-5.38, 5.29)	-1.26	(-6.19, 3.66)		-2.41	(-10.42, 5.59)	
Difference in change at 2 weeks (95% CI)	reference		-1.22	(-8.47, 6.04)	0.74	-2.36	(-11.99, 7.26)	0.63
Change from baseline to 3 mo (95% CI)	-10.62	(-16.27, -4.98)	-12.25	(-17.60, -6.89)		-24.31	(-33.45, -15.17)	
Difference in change at 3 mo (95% CI)	reference		-1.62	(-9.40, 6.15)	0.68	-13.68	(-24.42, -2.95)	0.01
Change from baseline to 6 mo (95% CI)	-1.00	(-16.72, -3.27)	-16.70	(-23.43, -9.97)		-25.20	(-39.15, -11.26)	
Difference in change at 6 mo (95% CI)	reference		-6.71	(-16.21, 2.80)	0.17	-15.21	(-30.69, 0.27)	0.05
Pain (range 0-100)								
Mean (SD) at baseline	15.9 (19.23)		13.51 (17.48)			16.67 (15.53)		0.47
Change from baseline to 2 weeks (95% CI)	11.83	(6.92, 16.75)	10.37	(5.84, 14.90)		11.85	(4.52, 19.18)	
Difference in change at 2 weeks (95% CI)	reference		-1.46	(-8.14, 5.22)	0.67	0.01	(-8.81, 8.84)	1.00
Change from baseline to 3 mo (95% CI)	2.81	(-2.37, 7.99)	5.18	(0.27, 10.09)		4.92	(-3.25, 13.10)	
Difference in change at 3 mo (95% CI)	reference		2.37	(-4.76, 9.50)	0.52	2.11	(-7.56, 11.79)	0.67
Change from baseline to 6 mo (95% CI)	7.96	(1.82, 14.10)	2.32	(-3.80, 8.43)		-0.85	(-13.52, 11.82)	
Difference in change at 6 mo (95% CI)	reference		-5.65	(-14.31, 3.02)	0.20	-8.81	(-22.89, 5.26)	0.22
Breast symptom (range 0-100)								
Mean (SD) at baseline	12.78 (12.88)		12.58 (14.58)			15.74 (17.26)		0.39
Change from baseline to 2 weeks (95% CI)	11.04	(7.01, 15.07)	11.20	(7.52, 14.88)		3.96	(-1.98, 9.90)	
Difference in change at 2 weeks (95% CI)	Reference		0.16	(-5.30, 5.62)	0.95	-7.08	(-14.26, 0.10)	0.05
Change from baseline to 3 mo (95% CI)	4.72	(0.49, 8.96)	6.80	(2.82, 10.79)		-0.42	(-7.04, 6.20)	
Difference in change at 3 mo (95% CI)	reference		2.08	(-3.73, 7.89)	0.48	-5.15	(-13.00, 2.71)	0.20
Change from baseline to 6 mo (95% CI)	9.59	(4.58, 14.60)	5.84	(0.82, 10.85)		-0.76	(-10.99, 9.47)	
Difference in change at 6 mo (95% CI)	reference		-3.75	(-10.84, 3.33)	0.30	-10.35	(-21.73, 1.03)	0.08

Table 1.

Arm symptom (range 0-100)								
Mean (SD) at baseline	13.3 (14.74)		10.9 (15.71)			18.4 (14.93)		0.01
Change from baseline to 2 weeks (95% CI)	11.41	(6.87, 15.95)	14.59	(10.38, 18.79)		14.38	(7.55, 21.20)	
Difference in change at 2 weeks (95% CI)	reference		3.18	(-3.01, 9.36)	0.31	2.97	(-5.23, 11.16)	0.48
Change from baseline to 3 mo (95% CI)	5.09	(0.31, 9.88)	5.73	(1.18, 10.29)		4.82	(-2.79, 12.43)	
Difference in change at 3 mo (95% CI)	reference		0.64	(-5.96, 7.24)	0.85	-0.27	(-9.26, 8.72)	0.95
Change from baseline to 6 mo (95% CI)	6.09	(0.42, 11.76)	12.81	(7.12, 18.50)		0.35	(-11.39, 12.08)	
Difference in change at 6 mo (95% CI)	reference		6.72	(-1.31, 14.75)	0.10	-5.74	(-18.77, 7.29)	0.39
Overall QOL (range 0-100)								
Mean (SD) at baseline	52.3 (20.83)		55.1 (19.72)			58.5 (18.13)		0.19
Change from baseline to 2 weeks (95% CI)	3.64	(-1.43, 8.72)	2.98	(-1.71, 7.67)		-2.23	(-9.80, 5.34)	
Difference in change at 2 weeks (95% CI)	reference		-0.67	(-7.58, 6.24)	0.85	-5.87	(-14.99, 3.24)	0.21
Change from baseline to 3 mo (95% CI)	3.84	(-1.51, 9.20)	3.31	(-1.80, 8.42)		8.59	(0.13, 17.04)	
Difference in change at 3 mo (95% CI)	reference		-0.53	(-7.93, 6.86)	0.89	4.74	(-5.26, 14.75)	0.35
Change from baseline to 6 mo (95% CI)	6.38	(0.02, 12.73)	4.82	(-1.59, 11.23)		3.26	(-9.88, 16.40)	
Difference in change at 6 mo (95% CI)	reference		-1.56	(-10.58, 7.46)	0.74	-3.11	(-17.70, 11.48)	0.68
Physical function (range 0-100)								
Mean (SD) at baseline	84.4 (14.37)		84.8 (11.92)			82.7 (14.91)		0.64
Change from baseline to 2 weeks (95% CI)	-3.04	(-6.51, 0.43)	-3.09	(-6.30, 0.12)		-8.21	(-13.45, -2.98)	
Difference in change at 2 weeks (95% CI)	reference		-0.05	(-4.78, 4.67)	0.98	-5.17	(-11.45, 1.11)	0.11
Change from baseline to 3 mo (95% CI)	-2.74	(-6.41, 0.92)	-3.85	(-7.33, -0.37)		-5.20	(-10.99, 0.60)	
Difference in change at 3 mo (95% CI)	reference		-1.11	(-6.16, 3.94)	0.67	-2.45	(-9.31, 4.40)	0.48
Change from baseline to 6 mo (95% CI)	-1.28	(-5.04, 3.08)	-5.31	(-9.68, -0.95)		-5.62	(-14.64, 3.41)	
Difference in change at 6 mo (95% CI)	reference		-4.04	(-10.20, 2.13)	0.20	-4.34	(-14.36, 5.68)	0.40

Table 2.

FP3-5

CHINA MULTICENTER STUDY OF SENTINEL NODE BIOPSY SUBSTITUTING AXILLARY NODE DISSECTION: CBCSG-001 TRIAL WITH 5 YEARS FOLLOW-UP

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Background/Purpose: Sentinel lymph node biopsy (SLNB) is a minimally invasive staging technique for clinically axillary negative breast cancer patients. The widely application of SLNB substituting axillary lymph node dissection (ALND) need the evidence of equal axillary recurrence and survival for patients with negative SLNs.

Methods: China multicenter study of SLNB substituting ALND for breast cancer - CBCSG-001 trial was conducted from Jan. 2002 to Jun. 2007, with 1,970 SLNB patients recruitment from 9 centers. The primary objectives were 5 years disease free survival (DFS) and complications between SLNB and ALND. The second objectives included 5 years overall survival (OS). Combined methylene blue dye and 99mTc-sulfur colloid or 99mTc-IT-Rituximab were used as tracers for SLNB. Preoperative lymphscintigraphy was mandatory for all patients. Patients with negative SLN did not receive ALND.

Results: The median age was 46 years. The median number of SLN was 2. Tumor size was less than 5cm, with mean size as 1.9 cm. The surgical types were as follows: breast conserving surgery (BCS)+SNLB 51.4%, mastectomy+SLNB 26.1%, BCS+ALND 8.9%, and mastectomy+ALND 13.6%, respectively. With a median follow-up of 60.3 months, the 5ys DFS and OS for the 1,672 patients with negative SLNs were 94.2% and 98.2%, respectively, while the complications of SLNB were significantly lower than that of

ALND ($p < 0.001$).

Conclusion: SLNB could replace ALND for SLN negative patients with low axillary recurrence, less postoperative complications, and improved quality of life. SLNB should be the standard of care for clinically axillary negative breast cancer patients.

FP3-6

EFFECT OF THE MIXED SOLUTION OF SODIUM HYALURONATE AND SODIUM CARBOXYMETHYLCELLULOSE ON UPPER LIMB DYSFUNCTION AFTER TOTAL MASTECTOMY: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL

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Background/Purpose: Restricted shoulder mobility is one of the major upper limb dysfunctions related with lower quality of life after breast cancer surgery. We evaluated the clinical efficacy and safety of the sodium hyaluronate carboxymethyl cellulose (HA-CMC) for prevention of upper limb dysfunction after total mastectomy (TM).

Methods: Ninety-nine women with breast cancer were allocated randomly into two groups. In HA-CMC group (n = 50), the mixed solution of HA-CMC was applied on the surface of pectoralis major muscle after TM while in control group (n = 49) TM was done in the standard fashion without the use of HA-CMC. The primary outcome was the range of motion (ROM) of shoulder and motion related pain which were measured before surgery (T0) and 3 (T1), 6 months (T2) after surgery. Secondary outcomes included disabilities of arm, shoulder and hand (DASH), and pectoralis minor length test (PMLT) by using Generalized Model (GLM) repeated measures.

Results: At baseline, no significant differences were found between the two groups. The shoulder flexion ROM was restricted at T1 (-11.2, $p < 0.001$) and T2 (-7.2, $p < 0.001$) comparing at T0 in HA-CMC group. As compared with controls, patients in the HA-CMC group had greater flexion ROM (difference 9.1 at T1, 10.8 at T2, $p < 0.001$). Similar patterns of results emerged for pain related with shoulder flexion, abduction and horizontal abduction. There are no significant effects of HA-CMC on DASH and PMLT. The safety profile of the patients was normal postoperatively.

Conclusion: These results demonstrated that HA-CMC is effective on upper limb dysfunction in patients undergoing TM by attenuating postoperative adhesion.

FP4-1

DEVELOPMENT OF NAVIGATION PROGRAM FOR NEWLY DIAGNOSED PATIENTS WITH BREAST CANCER IN KOREA

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Background/Purpose: Patients and caregivers of newly diagnosed with breast cancer may experience most highly physical, psychological and financial difficulties. The purposes of this study were to develop a navigation program for newly diagnosed with breast cancer patients and to evaluate its effects in Korea.

Methods: Based on the framework of Fillon et al., We developed a 'Navigation Program' for newly diagnosed with breast cancer patients. The patients were asked to complete self-administered questionnaires with satisfaction, distress, anxiety and depression before and after program implementation. Data collection was performed in Samsung Medical Center (SMC) from September 14 to December 20 2010.

Results: Navigation Program consisted of facilitating continuity of care (informational, management and relational continuity) and promoting empowerment of patients. We provided information-education package for informational continuity, the telephone counseling for management and relational continuity, and developed a self-care diary to promote patients' empowerment. A total of 91 patients were included in the study with 44 control and 47 experimental subjects. The mean scores of distress, anxiety and depression were decreased compared with baseline even though there was no statistical significance between the two groups. But the mean score of overall satisfaction of this program was 3.76 out of 5.

Conclusion: 'Navigation program in SMC' has applied concept of navigation into oncology clinical setting in Korea. Navigation program can play a significant role in assisting patients across the care continuum. More research is needed on the application of navigation program and systematic evaluation based on the objective outcomes.

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FP4-2

THE EFFICACY OF BREAST CANCER EDUCATION FOR JAPANESE YOUNG FEMALES

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Background/Purpose: The national average rate of breast cancer screening (BCS) is about 20% in Japan. Thus, we think that breast cancer education for young females is needed to improve the rate of BCS in the future. Therefore, we undertook an educational program to promote breast cancer awareness to raise awareness/understanding of breast examinations for young females and examined the effect.

Methods: Several breast specialists visited a number of universities to lecture on breast for female students. In addition, we distributed a 30-items questionnaire on the understanding of breast, changes in awareness of breast cancer examination, and changes in attitudes to life due to the lecture and analyzed whether interest in BCS and understanding of breast cancer were increased due to the breast cancer education program.

Results: We visited six institutes and lectured to a total of 580 female students. Their knowledge of breast (18 items) were deepened by the lecture ($p < 0.001$). According to the results of the questionnaire distributed after the lecture, 68% of female students replied that they wanted to take BCS regularly in the future, and 28% female students wanted to try BCS once. The ratio of female students who felt encouraged to take BSC by this lecture was 97%.

Conclusion: We were able to promote breast cancer awareness in young female students, and demonstrate the importance of continuing such education programs in the future.

FP4-3

EFFECTS OF COMBINED AEROBIC AND RESISTANCE EXERCISE PROGRAM ON QUALITY OF LIFE BREAST CANCER SURVIVORS IN IRAN

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Background/Purpose: Breast cancer is the most prevalent type of cancer in Iranian women. Exercise appears to diminish many of the side effects resulting from breast cancer and its treatment. However, very little research, examine outcomes of combined aerobic and resistance training exercise interventions on quality of life in breast cancer survivors in Iran. The purpose of this clinical trial study was to examine the effects of combined aerobic and resistance exercise program on quality of life breast cancer survivors.

Methods: Breast cancer survivors (n = 80) between 6 month to 2 years of completing treatment were randomly assigned to exercise group (n = 40; 44/6 ± 7/6) and control group (n = 40; 47/2 ± 10/7). The exercise group followed an 8-weeks exercise program consisting of three times per week of 60-min duration, supervised by an experienced investigator and divided into resistance exercises and aerobic training. Before and after the intervention period, quality of life (QOL) in both groups measured by Quality of Life Instrument - Breast Cancer Patient Version scale National Medical Center and Beckmam Research Institute.

Results: Data analysis revealed no significant difference in total score of QOL in both groups, although the QOL women in exercise group increase in psychological, social and spiritual domains and decrease in control group.

Conclusion: Combined aerobic and resistance exercise after completion of breast cancer therapy produces improvements in quality of life women.

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FP4-4

BONE LOSS IN BREAST CANCER SURVIVORS: PREVALENCE, RISK FACTORS, AND ASSOCIATION WITH QUALITY OF LIFE

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Background/Purpose: We performed this study to examine the prevalence and risk factors of bone loss, and their relevance to health-related quality of life (HRQOL) in breast cancer survivors.

Methods: A total of 136 disease-free breast cancer survivors (mean age, 50.1 years) were recruited from a comprehensive hospital in Korea. Subjects completed a self-reported measurement, which included the EORTC QLQ-C30 and Hospital Anxiety and Depression Scale, and bone mineral density (BMD) was determined with dual-energy X-ray absorptiometry.

Results: Among 136 breast cancer survivors, 49 women (36.0%) had osteopenia, and six women (4.4%) had osteoporosis. Univariate analyses revealed that older age, low level of education, low monthly income, menopause, aromatase inhibitor (AI) therapy, past or current smoking, and level of physical activity were associated with bone loss (BMD t-score < -1.0). Women who had a low level of monthly income (OR = 2.50, p = 0.020), experienced menopause (OR = 3.44, p = .049) and were past or current smoker (OR = 4.16, p = 0.031) were at increased risk for bone loss in multivariate analyses. In addition, women who had bone loss reported worse role functioning (p = 0.022) and higher level of anxiety than women who did not (p = 0.43).

Conclusion: Our study indicates a high prevalence of bone loss in breast cancer survivors of low economic status who have experienced menopause and who are a past or current smoker. Monitoring and treatment strategies to reduce bone loss risk are warranted in this population.

FP4-5

OVARIAN FUNCTION AND MENOPAUSE-SPECIFIC QUALITY OF LIFE IN PREMENOPAUSAL WOMEN RECEIVING ADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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Background/Purpose: Ovarian failure is a frequent sequel of adjuvant chemotherapy for the breast cancer and is known to influence the quality of life.

Methods: Serial blood samplings for hormone profiles and questionnaires were performed before the initiation of adjuvant chemotherapy (of adriamycin, cyclophosphamide ± taxane), at 4 mo, 10 mo, and 16 mo in 312 premenopausal breast cancer patients from October 2003 to July 2007.

Results: Higher incidence of long term chemotherapy related amenorrhea (CRA), defined as absence of menstruation ≥ 12 months was observed in older women (age ≥ 40 years) than younger women (age < 40 years), 77.4% vs 18.3% respectively (p = 0.001). The onset of amenorrhea after initiation of chemotherapy was 2 months in median (range; 0-13), and the median duration of temporary CRA was 7 months (range, 3-17). Decreased serum E2 (25.6 ± 33.4 pg/mL) and elevated FSH (51.5 ± 24.0 mIu/mL) were observed at 4 months afterward regardless of age. However, the levels of recovery varied depending on age. E2 recovery (131.2 ± 225.6 pg/mL) and FSH decrease (15.3 ± 16.9 mIu/mL) were prominent in younger women than older women (55.7 ± 123.9 pg/mL, 26.0 ± 20.9 mIu/mL, respectively) (p = 0.001, p = 0.002, respectively) at 10 months afterward. The menopause-specific quality of life (QoL) was worst at the end of chemotherapy. Psychosocial domain was the worst and influenced by menstrual status and exercise.

Conclusion: Long-term CRA was developed in 77.4% in women of aged ≥ 40 years. These menstrual changes affected QoL. Programs to support survivors' QoL are urgently needed especially for this group.

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FP5-1

SIMULTANEOUS PERTURBATION OF TGFBETA AND EGF SIGNALING REVEALS SHARED NETWORK IN REGULATION OF THE CELL PROLIFERATION

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Background/Purpose: Cell proliferation is controlled by stimulators and inhibitors acting simultaneously. This combined functionality is not a simple sum of individual pathways, but has novel properties and engage novel mechanisms.

Methods: We profiled a phosphoproteome after simultaneous perturbation of transforming growth factor-beta (TGFβ) and Epidermal Growth Factor (EGF) pathways, that inhibit (TGFβ) and stimulate (EGF) the cell proliferation.

Results: We identified convergence targets of TGFβ and EGF. Phosphorylation of in total 47 proteins was dependent on both growth factors, as compared to treatments with TGFβ or EGF alone. Systemic analysis of the convergence targets in the global gene network showed that the combined action engaged regulatory mechanisms associated not only with TGFb and EGF, but also with insulin signaling, VEGF, TNF, Wnt, mTOR, Toll, Jak-STAT, and response to hypoxia. Further analysis of ways for the phosphoprotein-dependent network to regulate the cell proliferation indicated that MEK1, CK1, GSK3β, TNFR, and ZAK kinase could be primary targets given the combined action of TGFβ and EGF. To validate involvement of the kinases detected in the network analysis, we manipulated their activities using kinase inhibitors. As predicted, inhibition of MEK1/MEK2 and CK1 affected TGFβ- and EGF-dependent regulation of cell proliferation.

Conclusion: Thus, the simultaneous perturbation of TGFβ and EGF showed that extracellular growth factors signal via a shared network, which supported the concept of signaling as a mechanism with many extracellular inputs into an integral densely connected intracellular circuitry.

FP5-2

PROMOTER METHYLATION OF RASSF1A MODULATES THE EFFECT OF MICROTUBULE-TARGETING AGENT, DOCETAXEL, IN BREAST CANCER

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Background/Purpose: Docetaxel is one of the most commonly used chemotherapeutic agents in breast cancer. To avert from significant toxicities, identification of predictive markers for response is one of the important unsolved clinical needs. Potential associations of RASSF1A hypermethylation and response to docetaxel-based chemotherapy were studied.

Methods: The expression of RASSF1A in breast cancer cell lines and tissues of normal breast, ductal carcinoma *in situ* (DCIS), and breast cancer (n = 45) was analyzed by immunohistochemistry, real time reverse transcriptase-polymerase chain reaction (RT-PCR), and Western blot. Using 5-aza-deoxycytidine, a demethylating agent, to reverse methylated genes in the breast cancer cells, the RASSF1A promoter methylation was evaluated by methylation-specific PCR (MSP). The effects of docetaxel and RASSF1A in cancer cells were evaluated by MTT assay, [3H]-thymidine incorporation assay, and cell cycle analysis.

Results: Immunohistochemical staining showed that the expression of RASF1A was frequently lost in primary breast cancers and human breast cancer cell lines, while normal breast tissues or DCIS displayed moderate to strong expression. Furthermore, MSP analysis revealed that RASSF1A was frequently methylated in primary breast cancers, and prospective analysis in patients with locally advanced or metastatic breast cancer showed that methylated RASSF1A was significantly more common in postmenopausal patients ($p = 0.029$) and in non-responders to docetaxel-induced chemotherapy ($p = 0.042$). Finally, in vitro studies showed that RASSF1A had cooperative activity in suppression

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of cancer cell growth and proliferation by enhancing docetaxel-induced cell cycle arrest.

Conclusion: Our results suggest that hypermethylated RASSF1A is an important factor modulating efficacy of docetaxel-based chemotherapy in breast cancer.

FP5-4

AURORA KINASE REGULATES TPA-INDUCED MMP-9 EXPRESSION IN MCF-7 BREAST CANCER CELLS

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Background/Purpose: Aurora kinase, a novel family of serine/threonine kinases, has been linked to tumorigenesis. Degradation of the extracellular matrix (ECM) and destruction of the basement membrane by cancer cell are the important processes for direct invasion. Matrix metalloproteinase-9 (MMP-9), which degrades the ECM, plays an important role in breast cancer cell invasion. Nuclear factor-κB (NF-κB), activator protein-1 (AP-1), and mitogen-activated protein kinase (MAPK) signaling pathways had been known to be involved in 12-O-tetradecanoy-phorbol-13-acetate (TPA)-induced MMP expression. This study has investigated whether aurora kinase regulates MMP-9 expression and invasion in MCF-7 breast cancer cells.

Methods: The expression of aurora kinases was analyzed by Western blotting. MTT assay was used for determination of cytotoxicity. MMP-9 expression was analyzed by gelatin zymography and MMP-9 mRNA level was analyzed by real-time PCR. Effect of aurora kinase on NF-κB/AP-1 DNA binding was analyzed by electrophoretic mobility shift assay (EMSA).

Results: TPA stimulation resulted in an up-regulation and phosphorlyation of aurora kinases. Treatment with MAPK inhibitors abolished TPA-induced aurora kinases up-regulation. Inhibition of the aurora kinases by reversine, aurora kinase inhibitor II, and VX-680 suppressed TPA-induced MMP-9 expression and invasion in MCF-7 breast cancer cells. RNAi targeting aurora kinases inhibited TPA-induced MMP-9 expression, too. In addition, activation of NF-κB, AP-1, and MAPK by TPA was suppressed by aurora kinase inhibitors.

Conclusion: Aurora kinase activation is one of the crucial steps in TPA-induced MMP-9 expression in MCF-7 breast cancer cells. This study provides new insight into the regulation of TPA-induced MMP-9 expression.

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FP5-5

UPREGULATION OF VEGF-A AND CD24 GENE EXPRESSION BY THE TGLI1 TRANSCRIPTION FACTOR CONTRIBUTES TO THE AGGRESSIVE BEHAVIOR OF BREAST CANCER CELLS

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Background/Purpose: The glioma-associated oncogene homolog 1 (GLI1) transcription factor is the terminal effector of the Hedgehog pathway, frequently activated in human breast cancers and an emerging target of breast cancer therapy. While somatic mutations in the human GLI1 gene have never been reported in any cell or tumor type, we recently discovered a novel alternatively spliced, truncated GLI1 (tGLI1) that has an in-frame deletion of 41 codons spanning the entire exon 3 and part of exon 4 of the GLI1 gene. Using glioblastoma models, we showed that tGLI1 has gained the ability to promote glioblastoma migration and invasion via its gain-of-function transcriptional activity. However, the pathological impact of tGLI1 on breast cancer remains undefined.

Methods: To address this knowledge gap, we undertook a series of biochemical analyses.

Results: We observed that tGLI1 is frequently expressed in breast cancer cell lines and primary specimens, but is undetectable in normal breast tissues and that tGLI1, but not GLI1, binds to and enhances the human VEGF-A gene promoter, leading to its upregulation. tGLI1-expressing breast cancer cells secret higher levels of VEGF-A and contain a higher propensity, than the isogenic cells with control vector and GLI1, to stimulate *in vitro* angiogenesis. Furthermore, tGLI1 has gained the ability to enhance the motility, invasiveness and anchorage-independent growth of breast cancer cells and that this functional gain is associated with increased expression of CD24, MMP-2 and MMP-9.

Conclusion: Our results define tGLI1 as a gain-of-function GLI1 transcription factor and a novel mediator of the behavior of clinically more aggressive breast cancer.

FP6-1

FACTORS ASSOCIATED WITH INVASIVE CARCINOMA IN THE PATIENTS DIAGNOSED WITH DUCTAL CARCINOMA *IN SITU* IN INITIAL BIOPSY

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Background/Purpose: In several patients initially diagnosed with ductal carcinoma *in situ* (DCIS), invasive carcinoma is founded in post-operative final pathologic finding. We evaluated factors associated final invasive finding in pre-operative DCIS patients.

Methods: This retrospective study was conducted for 93 patients treated at the Ewha womans medical center between January 2005 and May 2011 for DCIS in pre-operative biopsy. We compared group of patients whose final post-operative pathologic T stage were Tis (group A) with group of over T1mic (group B).

Results: Among 93 patients, 62 were classed as group A and 31 as group B. There's no significant difference in age, status of menopause and tumor size between two groups. 46 patients showed histological comedo type and 41.3% of them were group B. Among non-comedo type, 24.4% were group B. Histology type was not different between two groups. We also analyzed about hormone receptors and HER2/neu status. In post-operative findings, invasive carcinoma was found in 47.8% of estrogen receptor (ER) negative patients and 28.6% of ER positive patients. 53.3% of progesterone receptor (PR) negative, 24.2% of PR positive, 23.3% of HER2/neu negative and 65.4% of HER2/neu positive patients were group B. There is no significant difference in ER status between two groups, otherwise, in PR and HER2 status, they showed significant difference between two groups.

Conclusion: Results of this study suggest that PR negative or HER2/neu positive patients diagnosed with DCIS in pre-operative biopsy are more likely to be diagnosed with invasive carcinoma in post-operative final pathologic result than PR positive or HER2 negative patients.

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FP6-2

INTRADUCTAL MASS ON BREAST ULTRASOUND (US): FINAL OUTCOMES AND PREDICTORS OF MALIGNANCY

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Background/Purpose: We investigated the final outcomes of intraductal masses diagnosed on breast US and determined which clinical/radiologic variables may be associated with malignancy.

Methods: A total of 163 intraductal masses in 147 women with histologic data or ultrasound (US) follow-up (> 24 months) were included. Clinical/radiologic variables including patient age, symptom, lesion size, distance from the nipple and pathologic results were collected. US lesion appearance was reviewed and was classified into three types: a mass incompletely filling the duct, irregular mass or mass completely filling the duct, irregular mass extending outside the duct. Involvement of branch duct was also analyzed. Associations between clinical/radiologic variables and outcomes were analyzed by using Chi-square test and Student t test.

Results: Of 163 lesions, 72 lesions were surgically excised; 45, vacuum assisted biopsied; 35, core biopsied;11, followed with imaging. Thirteen (8%) masses were malignant (10 ductal carcinoma *in situ* and 3 invasive ductal carcinoma) and 150 masses were benign (84 papilloma, 8 atypical ductal hyperplasia, 32 fibrocystic diseases, 26 others). There was a significant difference in symptom, personal history ($p < 0.05$). Lesion US appearance was different between benign and malignant masses. Malignancies tended to fill the duct more completely or extend outside the duct with irregular surface ($p = 0.007$) and involve branch duct ($p < 0.001$) than benign. Mass size (≥ 1.5 cm vs. < 1.5 cm, 4/16 vs. 9/147, $p = 0.026$), and distance from nipple (≥ 1.5 cm vs. < 1.5 cm, 4/21 vs. 9/142, $p = 0.067$) were also associated with malignancy.

Conclusion: 8% (13/163) of intraductal masses are malignant. Symptom, personal history, lesion size, distance from nipple and US appearance can be predictors of malignancy.

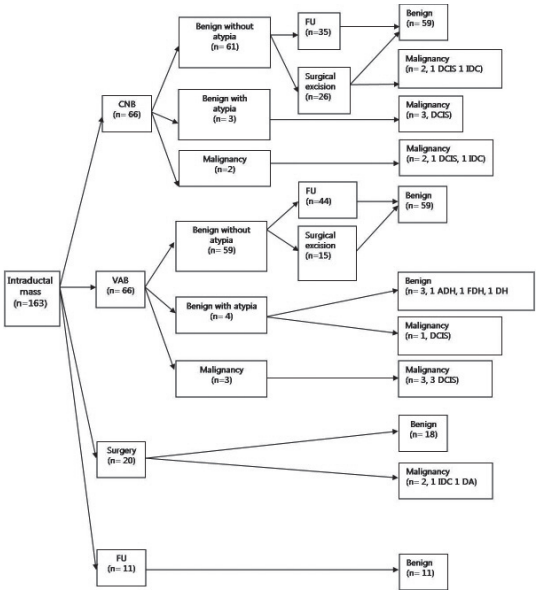

Fig. 1

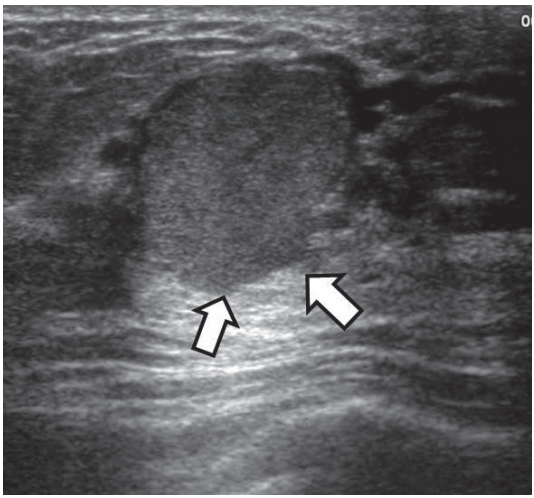

Fig. 2

Free Paper

FP6-3

SECOND-LOOK ULTRASOUND EXAMINATION FOR MRI-DETECTED BREAST LESIONS IN BREAST CANCER PATIENTS

Su Hyun Lee[1], Sun Mi Kim[2], Mijung Jang[2], Chae Yeon Lyou[2], Sung Won Kim[3], Eun Young Kang[3], So Yeon Park[4]

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Background/Purpose: To evaluate the value of second-look ultrasound (US) examination for additional enhancing breast lesions detected on MRI in breast cancer patients.

Methods: A retrospective review was performed of 964 patients who underwent bilateral MRI examinations for a preoperative staging of recently diagnosed breast cancer between May 2008 and April 2011. Of the 964 patients, 117 additional enhancing breast lesions (in 88 patients) were detected on MRI. Second-look ultrasound was performed and overall assessments were given. For lesions of suspicious for malignancy, histopathologic findings were confirmed by US- or MR-guided biopsy or lesion excision with needle localization. For probably benign lesions, imaging follow-up was used for benign histologic confirmation without biopsy. Pathologic results, MR findings and sonographic correlation was performed. Statistical analysis was performed with the Fisher exact test.

Results: Of 117 MR-detected lesions, 16 lesions (14%) (in 14 patients) were confirmed as additional cancers. Seventy-three lesions (62%) were sonographically correlated and included all 16 malignant lesions and 57 benign lesions. The other 44 lesions (38%) did not showed sonographic correlation and all lesions were nonmalignant lesions. Mass lesions identified on MRI were more likely to have a sonographic correlation than non-masslike lesions (71% vs. 38%, $p = 0.0015$). The sonographic finding of MR-detected malignant lesions were less suspicious and subtle and isoechoic parallel mass without echogenic halo or posterior acoustic feature were the most common finding.

Conclusion: Second-look ultrasound examination was useful for evaluation of additional suspicious lesions detected by MRI in breast cancer patients. Pathologic and MR findings of the lesions affected sonographic correlation.

FP6-5

ONE-STEP NUCLEIC ACID AMPLIFICATION (OSNA) FOR THE DIAGNOSIS OF SENTINEL LYMPH NODES OF BREAST CANCER - CHINA MULTICENTER STUDY CBCSG-001C

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Background/Purpose: With the widely application of sentinel lymph node (SLN) biopsy, there is an increasing need for the rapid and accurate intraoperative diagnosis of SLNs. CBCSG-001c was a prospective multicenter trial to validate the OSNA assay in China. The primary endpoint was the concordance rates of intraoperative OSNA assay with the in-depth permanent histological analyses based both on cases and SLNs.

Methods: From Feb. to Dec. 2010, 1188 SLNs from 552 breast cancer patients were enrolled from 5 centers. SLNs were cut into alternating ~2 mm blocks. One half of the blocks were sampled for H&E, with 4 sections each block. The other half was fully tested with OSNA.

Results: The concordance rate, sensitivity, and specificity were 89.1%, 87.7%, and 89.6%, repectively, based on the 552 cases, and 91.4%, 83.7%, and 92.9%, respectively based on the 1188 SLNs. Discordance were thought to be partly due to the sample error, and definition as histologically negative of ITCs. After discordant case investigation, the senstivity of OSNA assay was significantly higher than that of intraoprative frozen section and touch imprint cyctology.This quantitative molecular assessment allowed the distinction of the size of the metastasis, and the PPV of OSNA [++] for macrometastases was 83.2%.

Conclusion: As the largest OSNA study to date, our results, together with others, proved the OSNA assay to be a reliable and standardized tool for the intraoperative diagnoses of SLN as compared to the in-depth permanent histology, reducing the risk of second ALND, medical care costs and patients anxiety.

Free Paper

FP7-1

HER2 POSITIVE AND TRIPLE NEGATIVE SUBTYPES OF DUCTAL CARCINOMA *IN SITU*: IMAGING AND PATHOLOGIC FEATURES

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Department of Radiology, Seoul National Univ. Hospital, Korea

Background/Purpose: Gene expression profiling studies have identified intrinsic breast cancer subtypes (i.e. luminal, HER2+, and basal-like) that are distinctive in clinical outcome. The purpose of this study was to evaluate the imaging and pathologic features of DCIS according to the breast cancer subtypestroes.

Methods: During a 5-year period, a total of 206 women received the final surgical pathology diagnosis of pure DCIS. We divided into three subtypes by using immunohistochemistry: estrogen receptor (ER)-positive/HER2-negative, HER2-positive, and triple negative (TN, ER-/PR-/HER2-). HER2 receptor status was established by standardized methods and dichotomized as positive (DAKO score 3+ or HER2-amplification at FISH) or negative (DAKO score < 3+ or FISH negative). We reviewed DCIS lesions to assess mammography, MRI and pathology findings.

Results: Of the 206 DCIS, 112 (54%) were categorized as ER-positive/HER2-negative, 72 (35%) as HER2-positive, and 22 (11%) as TN. TN DCIS were less likely to be found by calcifications on mammography ($p = 0.02$). MRI findings of a mass lesion type ($p = 0.01$) and persistent enhancement pattern ($p = 0.03$) were more likely associated with TN DCIS. The large size (≥ 2 cm) ($p = 0.05$), high nuclear grade ($p < 0.01$), comedo necrosis ($p < 0.01$), high Ki-67 index ($\geq 10\%$) ($p < 0.01$) were more frequently associated with both HER2-positive DCIS and TN DCIS. The p53 positivity and bcl-2 negativity were more frequently associated with HER2-positive DCIS ($p < 0.01$).

Conclusion: TN DCIS are more likely to show non-calcified mammographic lesions, mass lesion type and persistent kinetics at MRI. Imaging findings of HER2-positive DCIS are similar to those of common DCIS. HER2-positive and TN DCIS are associated with aggressive pathologic features.

FP7-2

COMPARISONS THE NOMOGRAM TO OTHER PREDICTIVE TOOLS (ADJUVANT! ONLINE, ST. GALEN CONSENSUS, AND CS-IHC4) IN HORMONE RECEPTOR (HR)-POSITIVE BREAST CANCERS

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Background/Purpose: The aim of this study is to develop nomogram to predict recurrence and to decide adjuvant chemotherapy in hormone receptor (HR)-positive breast cancers. Then, we are to compare with order known predictive tools to evaluate the performance of our nomogram.

Methods: Data were collected from 1,070 postoperative HR-positive breast cancer patients between 2004 and 2007 at the Samsung Medical Center. We developed nomogram to predict recurrence based on Cox-regression multivariate analysis. To evaluate the performance of our nomogram, we compared the nomogram with other predictive tools (CS-IHC4, St. Galen consensus, and Adjuvant! Online) in our patients' cohort.

Results: According to Cox-regression model, estrogen receptor (ER) negativity, Ki67 index, and advanced stage were identified as independent risk factors for recurrence free survival. Nomogram showed an area under the receiver operating characteristic curve (AUC) of 0.69 (95% CI, 0.62-0.75). The nomogram score appeared to be closely correlated with CS-IHC4, St. Galen consensus, and Adjuvant! Online ($r = 0.668$, $p < 0.0001$ for CS-IHC4, $r = 0.642$, $p < 0.0001$ for St. Galen, $r = 0.656$, $p < 0.0001$ for Adjuvant! Online). Kaplan-Meier of RFS curves according to scores of the nomogram, CS-IHC4, Adjuvant! Online, and risk groups of St. Galen consensus showed significant discrimination in HR-positive breast cancers ($p < 0.0001$ for nomogram scores, $p < 0.0001$ for CS-IHC4, $p = 0.034$ for Adjuvant! Online, and $p = 0.001$ for risk groups of St. Galen consensus).

Conclusion: The nomogram based on Ki67 proliferative index may have greater clinical significance in HR-positive breast cancers and showed good correlations with CS-IHC4, Adjuvant! Online, and risk groups of St. Galen consensus.

Free Paper

FP7-3

P95HER2 AND PTEN AS SUPPLEMENTAL PREDICTIVE MARKERS TO ANTI-HER2 THERAPY: INTERIM ANALYSIS OF AN OBSERVATIONAL BIOMARKER STUDY

Soonmyung Paik[1], Gyungyub Gong[2], Yoon Sim Yap[3], Tae-you Kim[4], Gerardo Cornelio[5], Sung Bae Kim[2], Janice Tsang[6], Hyuk-chan Kwon[7], Ting-ying Ng[8], Jungsil Ro[9]

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Background/Purpose: Currently available anti-HER2 targeted therapies do not demonstrate efficacy in 100% of HER2-positive breast cancer (HER2+ BC) patients. Several reports suggested that there may be other predictive markers such as p95HER2 or PTEN, which could be useful adjunctive guidance towards personalized treatment selection.

Methods: We investigated HER2-relevant biomarkers in a prospective observational cohort of Asian HER2+ metastatic BC patients exposed to < 1 lines of anti-HER2 regimen who were initiated on lapatinib following disease progression. At interim analysis, tumor tissues from primary diagnosis were tested using immunohistochemistry (bioMerieux) for incidence of p95HER2 expression (defined as positive at 30% cut-off) and PTEN downregulation (defined relative to normal cells; Abcam, clone Y184 1:100). Futility was based on < 16% (8/50) of p95HER2 positivity rate among the study population.

Results: Of the 54 evaluable samples, 29 (53.7%) were p95HER2+ve and 22 (40.7%) were PTEN-ve. At data cut-off date of 12-Mar-2011, median follow-up time from initiation of lapatinib treatment was 12.36 weeks (0-46.29 weeks) with median progression-free survival (PFS) of 24.6 weeks and event rate of 26.7%. Figures 1 and 2 below show the PFS by (1) p95HER2+ve and (2) PTEN-ve status respectively: PFS was not statisti-

cally significant by estrogen receptor (ER) status (p = 0.556612), where 50% of the patients were ER+ve.

Conclusion: With 53.7% p95HER2 positivity rate, our study was above threshold for futility. Although still preliminary, the results suggest a trend towards clinical response to lapatinib in HER2+ metastatic BC irrespective of p95HER2 or PTEN status. Our study will confirm these findings using larger datasets at final analysis.

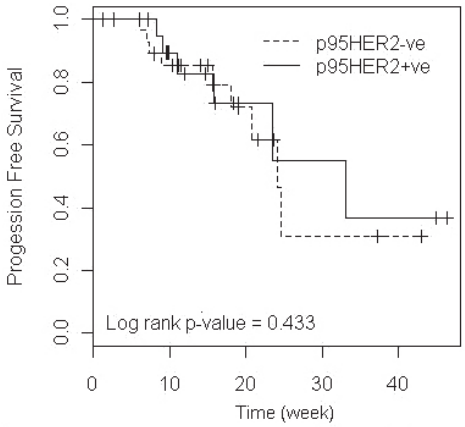

Fig. 1 Progression free survival (PFS) by p95HER2 status.

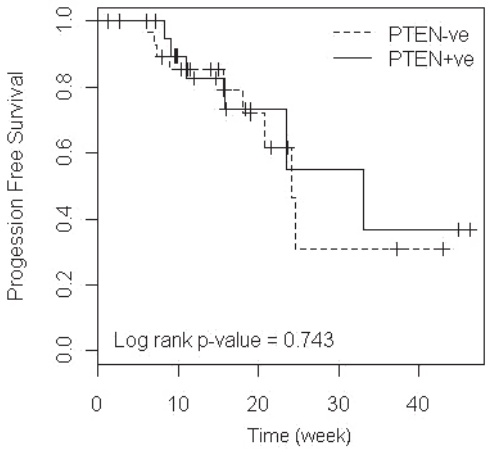

Fig. 2 Progression free survival (PFS) by PTEN status.

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FP7-4

PROPOSAL OF A BREAST CANCER-SPECIFIC PROGNOSTIC MODEL AND A NOMOGRAM TO PREDICT OUTCOMES FOR PATIENTS WITH BRAIN METASTASES (BM) FROM BREAST CANCER

Hee Kyung Ahn[1], Soohyeon Lee[1], Yeon Hee Park[1], Joo Hyuk Sohn[2], Jae-cheol Jo[3], Jin-hee Ahn[3], Kyung Hae Jung[3], Jin Seok Ahn[1], Sung-bae Kim[3], Young-hyuck Im[1]

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Background/Purpose: The purpose of this study was to validate the recently published Breast-GPA and to propose a new prognostic model and nomogram for patients with brain metastases (BM) from breast cancer (BC).

Methods: We retrospectively investigated 171 consecutive patients who were diagnosed with BM from BC between 2000 and 2008 at Samsung Medical Center. We appraised the recently proposed Sperduto's breast cancer specific GPA in our cohort and developed a nomogram to predict outcomes using multivariate Cox-regression analysis. By putting the Breast-GPA together with our nomogram, we developed a new prognostic model. We validated our new prognostic model with two independent external patient cohorts.

Results: The overall median survival time from BM in our cohort was 9.6 months. The Sperduto's breast cancer specific GPA did not accurately predict survival in our patient cohort. Based on our Cox-regression analysis, therapeutic effect of anti-HER2 agent (trastuzumab) and status of extracranial systemic disease control were incorporated into our new prognostic model after developing the nomogram. Our new prognostic model showed significant discrimination in MST with class I (n = 15) 3.7 months, class II (n = 82) 7.8 months, class III (n = 42) 10.7 months, and class IV (n = 32) 19.2 months ($p < 0.0001$). The new prognostic model did accurately predict survival of patients with BC from BM in two external validation cohorts ($p = 0.003$ and $p = 0.013$, respectively).

Conclusion: We propose a new prognostic model and a nomogram refelecting the different biological features of breast cancer including treatment effect and status of extracranial disease control which was validated in two independent external cohorts.

FP7-5

CHARACTERIZATION OF FUNCTIONING OF BREAST CANCER SURVIVORS USING ONLINE HEALTH CONSULTATION WITH THE HELP OF ICF

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Background/Purpose: Online health consultation serves an alternative source of information for breast cancer patients to cope with their dysfunctions across the cancer care continuum. This study is to assess characterization of function in patients with breast cancer using online health consultation with the help of the International Classification of Functioning, Disability, and Health (ICF).

Methods: A total of 928 requests posted by breast cancer survivors to an online health consultation. Q&A board during 2004 to 2010 were translated into ICF categories using NVivo software. All individual requests were digitally recorded and transcribed verbatim. Interview texts were divided into meaning units and the concepts contained in the meaning units were linked to the ICF according to established linking rules. Frequencies of identified ICF categories across the cancer care continuum were calculated.

Results: The most commonly discussed cancer- or treatment-related dysfunctions were sensation of pain (43.1%) and emotional function (36.3%). Structure of body structures such as breast and nipple (s6302) was more affected during treatment, while activities and participations were more problematic in the after-treatment phase. This included menstruation function (b650) and weight maintenance functions (b530) as well as assisting others (d660) and recreation and leisure (d920). Food (e1100) was the most frequently discussed environmental factor across cancer continuum.

Conclusion: For patients with breast cancer, anatomical changes are more discussed during treatment, while body functions and participation in every-day life are more problematic after treatment phase. Therefore, information and rehabilitation service should be provided according to their cancer continuum.

Free Paper

FP8-1

HEALING CANCER: SELF-HELP IN CYTOKINE MANAGEMENT THROUGH EXERCISE, STRESS MANAGEMENT, AND DIET THROUGHOUT THE CANCER CONTINUUM

Stellie Kim

Greater Bay Region, American Cancer Society, USA

Background/Purpose: The psychological devastation which impacts cancer patients during treatment is difficult to surmount. The feelings of powerlessness and hopelessness can interfere with cancer treatment. Caregivers and healthcare providers have responsibilities to empower patients and help take charge of cancer treatment by developing healthy lifestyles to boost immune health.

Methods: In several cancer support groups in the Bay Area, we studied 103 patients with a cancer diagnosis. Patients were introduced to art therapy to express and evaluate their initial psychological states. Participants learned to follow self-help guidelines in exercise plans, stress management techniques, and diet plans. The self-evaluations of active participants and non-participants were examined after the active cancer treatment.

Results: 51 patients out of 103 were complaint to the initial art therapy evaluation. All patients' self-images were severely distorted. Upon the completion of active treatment, 33 of them acknowledged to implementing some types of suggested self-help guidelines and activities in their lifestyles, which results in positive outcomes in their psyche. Self-help with support from the caregivers assisted 11 patients to be at ease with transitions.

Conclusion: Despite the fact that many patients feel and act powerless during their cancer treatment, psychological and behavioral changes of cancer patients to take control of their cancer journey with exercise, stress management, or special diets can produce positive outlooks during and after cancer treatment. Support from caregivers including clinicians plays a critical role in the positive mind shift of patients in the cancer control continuum.

FP8-2

EFFECT OF AN INTEGRATE BREAST HEALTH MANAGEMENT PROGRAM FOR PREGNANT WOMEN ON KNOWLEDGE, ATTITUDE, EARLY SCREENING PRACTICE ABOUT BREAST CANCER

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Background/Purpose: Breast cancer has become increasingly young age among Korean women. Women have the interest for their breast in pregnancy, to breast cancer prevention and management through the antenatal care could be an effective strategy during pregnancy. This study aimed to develop and evaluate an integrated breast health management program for the prevention of breast cancer of pregnant women.

Methods: This study employed a nonequivalent control group non-synchronized design (22 experimental, 29 control). Participants were pregnant women over 28 weeks. The integrated breast health management program focuses on the breast management during breast-feeding and the education about the prevention and early screening of breast cancer.

Results: At the early postpartum period, there were statistically significant differences in knowledge and attitude about breast cancer between before and after the program. There were statistically significant differences in breast self examination at 6 months and 12 months after delivery. There were also significant differences in mammogram at 12 months after delivery. However, there were no statistically significant differences in clinical breast examination and breast ultrasonogram at 6 months and 12 months after delivery. The integrated breast health management program was effective in increasing knowledge, attitude, and early screening practices among pregnant women.

Conclusion: In this study, we showed that it is effective to provide an intervention about breast cancer to pregnant women especially when their interest in breast is high such as breast-feeding period. We conclude that the breast health management program for pregnant women should be provided differently for each phase of pregnancy and delivery.

Free Paper

FP8-3

THE CHARACTERISTICS OF BREAST CANCER IN WOMEN OVER THE AGE OF 80

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Background/Purpose: In Japan the number of breast cancer patients is increasing and the most common age groups are the 40s and-50s. Recently, breast cancer treatment is based on the biological features of the tumor. In contrast, elderly breast cancer patients have more incidences of comorbidity, and therefore the treatment for elderly patients can't always be decided on tumor biology. A survey of the breast cancer characteristics in elderly patients over the age of 80 was conducted to determine the appropriate treatment.

Methods: Between July, 1994 and March, 2011, 171 breast cancer patients aged 80 years or older were analyzed. The therapeutic approach, the clinical and histological findings were compared with younger patients under 80.

Results: Treatment for the patients fell into three categories: observation (13 cases), surgery (130 cases), and systemic therapy. Endocrine therapy was performed in 89 cases, chemotherapy in 2 cases, and trastuzumab in 3 cases. There was no difference in tumor size and lymph node metastasis between the two age groups; however, the elderly patients had more distant metastases. The estrogen receptor and progesterone receptor positive rate was 75% and 56% in elderly patients, respectively. These values were similar to the younger patients, but the HER2 positive rate and Ki-67 value was lower in the elderly patients. The 5-year disease free survival was 91.6% and overall survival was 60.2%.

Conclusion: The characteristics of breast cancer in patients over the age of 80 indicate lower grade of malignancy. Moreover, operation and endocrine therapy might be effective for disease control.

FP8-4

QUALITY OF LIFE AND SYMPTOM EXPERIENCE IN BREAST CANCER SURVIVORS AFTER PARTICIPATING IN A PSYCHOEDUCATIONAL SUPPORT PROGRAM: A PILOT STUDY

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Background/Purpose: Post-treatment survivorship has not been extensively studies despite long-standing evidence that after breast cancer treatment, women need continuing support to deal with their physical and psychosocial concerns. The purpose of this experimental pilot study was to examine the QOL and symptom outcomes of a psychoeducational support program for women in the first year of post-breast cancer treatment survivorship.

Methods: The sample consisted of 48 female breast cancer survivor randomly assigned to an intervention group (n = 25) and control group (n = 23). The 12-week psychoeducational support program consisted of individual face-to-face education using a participant handbook, telephone delivered health coaching sessions, and small group meetings. Study instruments were The Memorial Symptom Assessment Scale Short Form and Functional Assessment of Cancer Therapy-Breast questionnaire. Measurement was performed at baseline (pre-test), after intervention (post-test) and at 3-months after intervention (follow-up test). In data analysis, analysis of variance of repeated measures was used.

Results: Compared with the control group, survivors in the intervention group reported higher quality of life overall and higher emotional well-being. The intervention group reported lower psychological symptom distress than the control group.

Conclusion: A psychoeducational support program may promote a better overall quality of life and symptom experience in transition to survivorship among female breast cancer survivors. Implications for practice: Oncology nurses are in a position to provide education and support to assist breast cancer survivors in managing their symptom and adjusting to life after primary treatment. Research to determine optimal strategies to improve breast cancer survivors' overall health and quality of life is needed.

Free Paper

FP8-5

EFFECTIVENESS OF EXPRESSIVE WRITING PROGRAM FOR WOMEN WITH BREAST CANCER IN KOREA

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Background/Purpose: Cancer is a traumatic event, so people with cancer perceive a cancer as a stressor and tend to have a difficulty of expressing their cancer-related emotions such as anxiety, sadness, and anger. If these emotions were suppressed, it could effects negatively on their cancer recovery and quality of life. It is necessary to develop interventions that could help people with cancer express their emotions. The expressive writing about the traumatic events has been recognized as a useful intervention for the lay people in decreasing physical and psychological symptoms and increasing QOL, by regulating emotion and intrusive thoughts. The purposes of this study were to develop and to examine expressive writing program's effects on stress physical symptom, cancer symptom, anxiety, depression, and QOL in women with breast cancer.

Methods: Non-equivalent control pre-post design was used. Number of participants was 29 for each group. Data were collected from January to July in 2010 using questionnaires.

Results: Results of the study were: 1) Significant decrease in stress physical symptoms ($p < .00$) and a significant increase in quality of life ($p = .024$) between the experimental and the control groups. 2) No significant differences in cancer symptoms, anxiety, and depression between the experimental and the control groups.

Conclusion: It would be helpful to conduct a study for women with breast cancer with the above average level of anxiety and depression. The result of the study demonstrates that the expressive writing program to express cancer-related deep thoughts and emotions could help in decreasing physical symptoms and improving quality of life.

GBCC2011

Poster Discussion

PO01-01

THE PREVALENCE OF BRCA MUTATION AMONG FAMILIAL BREAST CANCER PATIENTS IN KOREA: RESULTS FROM KOREAN HEREDITARY BREAST CANCER STUDY

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Background/Purpose: Primary aim of this study is to estimate the prevalence of BRCA1/2 mutations among familial breast cancer (BC) patients in Korea.

Methods: We analyzed 775 familial BC patients who were enrolled in the Korean Hereditary Breast Cancer (KOHBRA) study from 36 institutions between May 2007 and May 2010. Familial BC is defined as BC patients with a family history of BC or ovarian cancer (OC) in any relatives. All probands received genetic counseling and BRCA genetic testing was then performed after informed consent. This study is approved by institutional review board.

Results: Mean age at diagnosis of BC was 43.6 years old. The number of probands with family history of BC only and OC was 682 and 93, respectively. Overall prevalence of BRCA mutation among familial BC patients is 21.7% (BRCA1 9.3% and BRCA2 12.4%, respectively). Subgroup analysis showed the prevalence of BRCA mutation as follows;

19.6% among patients with BC family history only (BRCA1 7.6% and BRCA2 12.0%, respectively) and 36.6% among patients with OC family history (BRCA1 21.5% and BRCA2 15.1%, respectively). Most of the subgroup satisfied the 10% probability criteria to undergo BRCA testing. However, the prevalence of BRCA mutation among the subgroup, with two BC patients in a family with probands age at BC diagnosis older than 50 years old, was only 7.1%.

Conclusion: Korean familial BC patients are a good candidate for BRCA testing even with single- or 3rd degree relative-breast cancer family history. However, the probands age at diagnosis should be carefully considered when selecting a patient.

PO01-02

CLIMACTERIC SYMPTOMS AND MENOPAUSAL MANAGEMENT IN PREMENOPAUSAL BREAST CANCER PATIENTS WHO UNDERWENT ADJUVANT THERAPY

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[2]*Department of Surgery, Seoul St. Mary's Hospital, Korea*

Background/Purpose: Climacteric symptoms are very common in post-treatment breast cancer patients. The purpose of this study was to compare climacteric symptoms and menopausal management in premenopausal breast cancer patients who underwent adjuvant therapy.

Methods: 89 breast cancer patients who had completed surgery and adjuvant therapy (chemotherapy, endocrine therapy and chemotherapy plus endocrine therapy), and had menses at the time of surgery were recruited. The instruments used in this study were the Functional Assessment Cancer Therapy-Breast plus Endocrine Symptom (FACT-ES) and menopausal management scale.

Results: The mean age of patients was 44.7 years. In 65 (77.4%) women amenorrhea occurred within 3 month since beginning adjuvant therapy. Among the 19 FACT-ES items, 'I have cold sweats' had the highest score (2.33 out of 4 point scale), and menopausal management has 21 item, 'Try not to smoke' had the highest score (3.60 out of 4 point scale). The mean score of the climacteric symptoms and menopausal management were no significant difference in types of adjuvant treatment. But the mean score of the climacteric symptoms in breast cancer patients who underwent chemotherapy plus endocrine therapy (1.44 ± 0.70) was higher than that of the other treatments. The mean score of the menopausal management in breast cancer patients who underwent chemotherapy was highest (2.84 ± 0.42). The correlation between the BMI and climacteric symptoms was positive ($r = 0.267$, $p = 0.013$).

Conclusion: Climacteric symptoms and menopausal management should be considered in developing nursing intervention for breast cancer patients who underwent adjuvant therapy. So the nurses should inform the patient so that they cope with their treatment well.

Poster Discussion

PO01-03

FACTORS AFFECTING THE DECISION OF RISK-REDUCING SALPINGO-OOPHORECTOMY AMONG PATIENTS WITH BRCA CARRIERS

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Background/Purpose: The objective of this study was to identify factors that may affect a BRCA mutation carrier's decision to undergo risk-reducing salpingo-oophorectomy (RRSO).

Methods: We identified 85 female BRCA mutation carriers from prospective genetic counseling database in Seoul National University Bundang Hospital. Patients underwent genetic counseling and testing after informed consent between May 2003 and December 2010. We used the probability of 0.1 (p-value) as the criteria for statistical significance.

Results: Of the 85 BRCA mutation carriers, 8 patients were excluded and 77 patients were included for the final analysis. Mean age of the study subjects was 45.1 and 13 patients (16.9%) underwent RRSO. Of the 77 patients, 56 patients (72.7%) were diagnosed as breast cancer (BC). Univariate analysis showed that the BC diagnosis was the only statistically significant factor for the decision of RRSO (23.2% for BC vs. 0% for unaffected, $p = 0.015$). To identify the factors affecting the decision of RRSO among BC patients, we analyzed 56 BC patients. Univariate analysis showed that family history of breast or ovarian cancer (28% for yes vs. 0% for none, $p = 0.098$), type of surgery (32% for breast conservation surgery vs. 8.7% for total mastectomy, $p = 0.091$), estrogen receptor (ER) status (39.1% for positive vs. 13.0% for negative) and progesterone receptor (PR) status (39.1% for positive vs. 13.6% for negative, $p = 0.053$) are statistically significant factor for the decision of RRSO among BC patients.

Conclusion: Diagnosis of breast cancer, family history of breast/ovarian cancer, type of surgery, and ER/PR status are important factors for the decision of RRSO among Korean BRCA carriers.

PO01-04

THE ASSOCIATION BETWEEN PARITY AND BREAST CANCER CHARACTERISTICS

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Background/Purpose: Epidemiologic studies showed that pregnancy is associated with reduced risk of breast cancer. We therefore hypothesized that parity may be differentially correlated with the risk of different subtypes and characteristics of invasive breast cancer.

Methods: We reviewed clinical, radiological and pathological records of women diagnosed with invasive ductal carcinoma of the breast at Samsung Medical Center between 2005 and 2009. Clinicopathologic results were assessed by Chi-square and Fisher's exact test with a Bonferroni correction for categorical variables and and the Kruskal-Wallis test for non- parametric continuous variables. A multinomial logistic regression model was used for multivariate analysis.

Results: Among a total of 2,897 patients, 266 (9.18%) patients were nulliparous. On univariate analysis, pregnancy was associated with old age ($p < 0.001$), high pN stage ($p = 0.035$) and expression of HER2 ($p = 0.006$). Multivariate analysis showed that only old age and expression of HER2 factors were associated with pregnancy. In the analysis between parity and molecular subtypes, parity also had a variable influence on the four ($p = 0.016$) and six ($p = 0.035$) breast cancer subtypes, depending upon the classification scheme.

Conclusion: Parity as a breast cancer risk factor differed by hormone receptor and HER2 expression. It seemed that parity might have a protective effect in hormone receptor-positive breast cancer, especially cancers expressing HR+ and Ki-67. Further studies to define and understand this result are needed.

PO01-05

DECISION MAKING FOR BREAST/OVARIAN CANCER RISK-REDUCING SURGERY

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Background/Purpose: Risk-reducing mastectomy (RRM) and risk-reducing oophorectomy (RRO) have known preventive efficacy in at-risk women. However, the surgeries are controversial because of potential intra-operative complications and post-surgery sequelae; thus decision-making for surgeries may not be straightforward for at-risk women. The purpose of this research was to describe specific surgery decisions of at-risk women and factors affecting their surgery decisions.

Methods: 107 women were enrolled from a university or a community cancer genetic risk program in Arizona, USA. After receiving initial genetic counseling and assessment, participants completed a survey on surgery decisions and factors affecting surgery decisions. BRCA test results were accessed from participants' genetic counselors.

Results: Most had a history of cancer and a negative BRCA test result. 47.7% had or planned to have surgery, 40.2% decided against surgery, and 12.1% were undecided. The main factors affecting decision for having surgery were information about personal risk of cancer, information about the risks and benefits of surgery, and coverage of health insurance. The main factors affecting decision against surgery were genetic testing results, information about personal risk of cancer, and not wanting any more surgery. The main factors affecting indecision were the irreversible nature of the surgery, the unconvincing genetic test results, and not wanting any more surgery. Decision with prophylactic oophorectomy was significantly associated with occupation and age.

Conclusion: To make their decision, participants used information, BRCA test results, and professional opinion. The findings may be useful for understanding surgery decisions of at-risk women and developing strategies for assisting women's decisions for risk-reducing surgery.

PO01-06

BARRIERS TO SEEKING DIAGNOSIS AND TREATMENT FOR BREAST CANCER IN A SELECTED PHILIPPINE POPULATION

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Background/Purpose: A study focusing on clinical breast examination (CBE) found that 34% of women referred to secondary care did not report to hospitals even when the cost of diagnosis and treatment were shouldered by a third party. This study aims to determine reasons for non-compliance to referral.

Methods: Fifty-eight women found with breast lump were interviewed using a questionnaire based on the health belief model (HBM). A 6-item Likert scale was used for the responses. Factor analysis with varimax rotation confirming the groupings of variables. T-test was used to compare average scores on the Likert scale. Logistic regression was done to determine independent factors affecting outcome.

Results: The barriers that were associated with non-compliance were perceived inconvenience ($p = 0.015$), (lack of) knowledge (0.048), fear ($p = 0.089$) and number of barriers ($p < 0.001$). Factors affecting compliance were number of barriers (OR = 2.17; 95% CI: 1.18-3.97), and inconvenience (OR = 1.53; 95% CI 1.0-2.32).

Conclusion: Non-compliance to referrals may be due to perceived inconvenience, fear and lack of knowledge. Efforts should be made to reinforce breast cancer awareness, and women encouraged to consult for possible cancer related symptoms.

Poster Discussion

PO01-08

PREVALENCE OF BRCA1 AND BRCA2 MUTATIONS IN NON-FAMILIAL BREAST CANCER PATIENTS WITH HIGH RISKS IN KOREA: THE KOREAN HEREDITARY BREAST CANCER (KOHBRA) STUDY

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Background/Purpose: The purpose of this study as a subset of the Korean Hereditary Breast Cancer (KOHBRA) study was to evaluate the prevalence of BRCA1 and BRCA2 mutations in non-familial breast cancer patients with high risk factors in Korea.

Methods: A subset of 758 patients was selected for this study from the KOHBRA cohort between May 2007 and May 2010. Mutations in BRCA1 and BRCA2 genes were tested using either F-CSGE, DHPLC or direct sequencing.

Results: Mutation of BRCA1/2 genes were identified in 65 (8.6%) patients [BRCA1

mutation: 25 (3.3%), BRCA2 mutation: 40 (5.3%)]. According to high risk groups, mutation of BRCA1/2 genes were identified in 53 (8.5%) of 625 early-onset patients (age ≤ 40 years), in 22 (17.7%) of 124 patients with bilateral breast cancer, in 3 (50.0%) of 6 breast and ovarian cancer patients, in one (5.9%) of 17 male breast cancer patients, in 4 cases (6.1%) of 66 multiple organ cancer patients, and in 18 (22.8%) of 79 patients having two or more of these high risk factors. The most common mutation was 509C > A for BRCA1 and 7708C > T for BRCA2. BRCA mutation of both the age < 35 years and the age ≥ 35 years groups did not show a difference among patients with other risks (25.93% vs. 22.92%, p = 0.78), however, was significantly different in patients without any other risk (9.96% vs. 2.87%, p < 0.001).

Conclusion: BRCA mutation for non-familial Korean breast cancer patients was detected at a high rate particularly, in patients with an earlier onset, bilateral breast cancer, breast and ovarian cancer, and two or more high risk factors.

PO01-09

EFFECTS OF FORGIVENESS EDUCATIONAL PROGRAM ON FORGIVENESS, SELF-ESTEEM, DEPRESSION, AND SPIRITUAL WELL-BEING IN MIDDLE AGED WOMEN WITH BREAST CANCER

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Background/Purpose: The purpose of this study was to identify the effects of Forgiveness educational program on forgiveness, self-esteem, depression and spirit ual well-being in middle aged women with breast cancer.

Methods: The research design was nonequivalent control group design with pre-test and post-test. 30 participants were selected from the new members of S breast cancer support group, who were receiving chemotherapy after mastectomy for breast cancer in one hospital in Busan, South Korea. Fifteen participants in an experimental group received Forgiveness educational program intervention and 15 participants in a control group did not receive the above intervention. The instruments for the research were the Forgiveness scale used by Yoon (2004), the Self-esteem scale developed by Rosenberg (1965). The depression scale developed by Spielberger (1995), and the Spiritual well-being scale developed by Paloutzian and Ellison (1982).

Results: The first hypothesis, 'the experimental group would have higher degree of forgiveness state than control group' was supported ($z = -3.496$, $p = 0.001$). 'The second hypothesis, 'the experimental group would have higher degree of self-esteem state than control group' was supported ($F = 12.381$, $p = 0.002$). The third hypothesis, 'the experimental group would have lower degree of depression state than control group' was supported ($F = 15.449$, $p < 0.001$). The fourth hypothesis, 'the experimental group would have higher degree of spiritual well-being state than control group' was supported ($F = 19.394$, $p < 0.001$)

Conclusion: Forgiveness educational program was effective on forgiveness, self-esteem, depression and spiritual well-being of middle aged women with breast cancer. Therefore, it is expected that it can be used not only for middle aged breast cancer patients, but also for various patients, their families, and clinicians.

PO01-11

CHARACTERISTICS OF BRCA1/2 MUTATION BREAST CANCER IN KOREA: COMPARED TO BREAST CANCER OF KOREAN BREAST CANCER SOCIETY REGISTRY

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Background/Purpose: The BRCA1/2 mutation cancer is about 5% of all breast cancer in Korea. In previous study in other country, BRCA1 breast cancer showed different characteristics unlike sporadic breast cancer. However BRCA2 breast cancer was demonstrated to be similar to sporadic cases. This study was done to investigate the clincopatholgic characteristics of BRCA1/2 breast cancer in Korea.

Methods: BRCA1/2 mutation cancer patients (n = 237) were enrolled by the Korean Hereditary breast cancer (KOHBRA) study. Data of compared breast cancer patients (n = 59,029) were provided by Korean Breast Cancer Society registry committee. Though retrospective medical records, the clinicopathologic review was performed.

Results: Compared to registry data, BRCA1 breast cancer had high nuclear and histologic grade (HG3 = 70.4%, NG3 = 62.3%; $p < 0.001$). They showed low portion of *in situ* carcinoma(0.9%; $p = 0.003$), more hormone receptor negative cases (estrogen receptor (ER)(-) = 82.2%, progesterone receptor (PR)(-) = 81.3%; $p < 0.001$) and lower proportion of Her2 over-expression(73.8%; $p < 0.001$). Therefore triple negative breast cancer was shown more frequently (70.4% ; $p < 0.001$). On BRCA2 breast cancer, most of characteristics were similar to registry data except more frequent axillary node involvement [BRCA2 cancer (50.9%) versus registry data (36.3%), $p < 0.001$] Generally, axillary node involvement was more frequent according to increasing tumor size. But BRCA1/2

breast cancer did not show the correlation between tumor size and axillary node involvement.

Conclusion: Triple negative breast cancers were shown more frequently in BRCA1 breast cancer. However, BRCA2 breast cancer was shown to be similar characteristics to sporadic breast cancers. And there was no correlation between tumor size and axillary lymph node involvement in BRCA1 or BRCA2 breast cancer.

PO02-01

OBESITY AND BREAST CANCER RISK IN KOREA ACCORDING TO MENOPAUSAL STATUS: META-ANALYSIS

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Background/Purpose: The incidence of breast cancer in Korea is rapidly increasing recently. Body mass index (BMI, kg/m^2) is one of the risk factors of breast cancer, especially in the postmenopausal women. In Korea, about sixty percents of breast cancer patients are premenopausal status. So the role of obesity would be different to the western country. We undertook a meta-analysis to verify the relation between BMI and breast cancer risk according to the menstrual status.

Methods: We retrieved the Korean literature using PubMed (http://www.pubmed.org/) and KoreaMed (http://www.koreamed.org/) database concerning the relationship between BMI and breast cancer in Koreans from 1994 to 2008. BMI more then 24 kg/m^2 was categorized as high. The overall effect size was represented by common odds ratio (OR). Heterogeneity test, sensitivity test and Egger's test of publication bias was conducted.

Results: The materials were fourteen studies with a total 5,534 breast cancer cases and 6,333 controls. The overall common OR (95% confidence interval) was 1.42 (1.25-1.61). The OR of postmenopausal women was 1.41 (1.19-1.68) and the OR of premenopausal women was 1.34 (1.13-1.59).

Conclusion: This study shows that the high BMI is the risk factors of breast cancer in Korea, regardless of menopausal status.

PO02-02

META-ANALYTIC COMPARISON OF BREAST CANCER RISK IN DIABETIC WOMEN: IMPORTANT DIFFERENCES BETWEEN ASIAN AND CAUCASIAN WOMEN SUGGEST RISK MANAGEMENT STRATEGIES

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Background/Purpose: Studies examining the association between type 2 diabetes and the risk of breast cancer in women have small sample sizes and inconclusive results. This study systematically reviews the risk of breast cancer in diabetic women and compares the risk of breast cancer in Caucasian and Asian women with type 2 diabetes.

Methods: Data for this meta-analysis were extracted from MEDLINE and EMBASE databases from years 1975 to 2010. Initial search of risk of breast cancer in women with type 2 diabetes yielded 33 studies. Out of the 33 studies found in the search, 22 studies met the inclusion criteria with 16 and 6 studies involving Caucasian and Asian women with a risk of breast cancer, respectively.

Results: The 22 studies analyzed using STATA® SE version10 involved a total of 77,204 women (47,083 Caucasians and 30,121 Asians). Meta analysis results showed that overall, women with type 2 diabetes had a 30.5% significantly higher risk of breast cancer (RR, 1.305; 95% CI, 1.30-1.31). Compared to Western women, Asian women with type 2 diabetes had 51.9% significantly higher risk of developing breast cancer (RR, 1.519; 95% CI, 1.508-1.530).

Conclusion: The study shows that women with type 2 diabetes were likely to be, as a group, at increased risk for breast cancer, with a relatively higher risk among Asian women. The efficacy of enhancements in glycemic control management, improving insulin sensitivity with exercise and diet control and screening for breast cancer particularly in Asian women with type 2 diabetes warrants further study.

PO02-04

A COMPARISON OF DISTRESS DUE TO ALTERED APPEARANCE IN BREAST CANCER SURVIVORS AND IN THE GENERAL POPULATION

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Background/Purpose: This study aimed to examine the distress due to altered appearance in breast cancer survivors compared with general population.

Methods: A cross-sectional survey was done with the breast cancer survivors and general population at the community event which held at 23 different areas in Korea. We assessed severity of altered appearance (body change, hair loss, skin change) and distress due to altered appearance.

Results: There were 536 breast cancer survivors and 329 women who did not have breast cancer. 39% and 17.5% of the survivors were receiving active (chemotherapy or radiotherapy) and passive (hormonal therapy) treatment respectively at the time of survey, and 11.8% of them were 2-5 year survivors and 13.8% were 5 years or longer survivors. Patients who were in current treatment experienced almost double amount of body change, hair loss, and skin change compared to the general population. Yet, patients who received active treatment experienced similar altered appearance compared to patients who received passive treatment and 2-5 year survivors. Long-term survivors (5 year or longer) experienced similar level of altered appearance compared to the general population (Table 1). Although patients who received active treatment more experienced altered experience compared to patients who had finished treatment, they had less distress due to the altered appearance (Figure 1).

Conclusion: Breast cancer survivors experience various altered appearance throughout the treatment and it lasted relatively long time. It is necessary to investigate effect of distress due to altered appearance on patients' quality of life and clinical outcome.

Poster Discussion

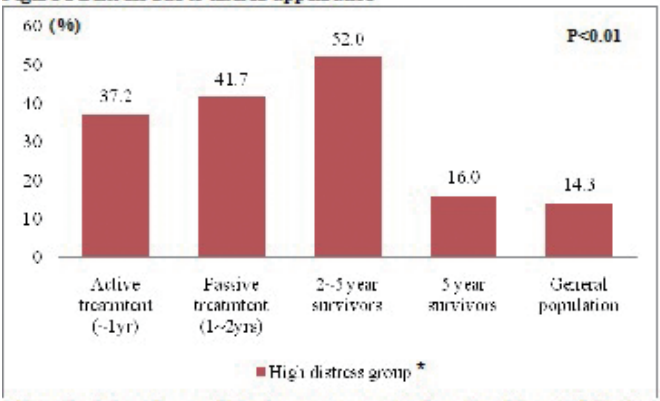
Table 1 Severity of altered appearance

Altered-appearance (range 1~10)	Active treatment (~1yr) N (%) 164 (19.0)	Passive treatment (1~2yrs) N (%) 151 (17.5)	2~5 year survivors N (%) 102 (11.8)	5 year survivors N (%) 119 (13.8)	General population N (%) 329 (38.0)	P-value
Body Mean (SD)*	6.5 (2.6)	6.4 (2.5)	6.0 (2.3)	3.3 (2.2)	3.2 (2.4)	<0.01
Alopecia Mean (SD)*	7.6 (3.2)	7.0 (3.6)	6.6 (3.4)	2.4 (2.3)	1.8 (2.1)	<0.01
Skin Mean (SD)*	6.4 (2.8)	5.8 (2.6)	5.0 (2.6)	3.1 (2.6)	2.6 (2.2)	<0.01

* For calculation of mean following each categories is assigned in each following value: 'None=1, Moderate=5, Severe=10' on altered appearance scale thus higher mean, higher changes.

Table 1.

Figure 1 Distress due to altered appearance



* For calculation of mean following each categories is assigned in each following value: 'None=1, Moderate=5, Severe=10'. A score of 5 or above (of 10 possible point) suggests high distress due to altered appearance.

Fig. 1

PO02-05

30-YEAR CHANGES IN BREAST CANCER INCIDENCE OF PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN OF ALL RACES IN UNITED STATES

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Background/Purpose: Breast cancer (BC) is the most common cancer in women. Globally, an estimated of > 1 million cases and 600,000 mortality occurring annually. In U.S., an estimated of > 200,000 new cases and 40,000 deaths occurred in 2010. BC incidence varies due to age, race and physiological factors. This study examined the trend in BC incidence of premenopausal (PreM) and postmenopausal (PostM) women of all races in U.S. from 1978-2008.

Methods: Data from nine cancer registries of the U.S. Surveillance, Epidemiology and End Results (SEER) Program that represent about 10% of the U.S. population were used. The incidence rate (AIR) of all races (Caucasian, Blacks, others) age-adjusted to the 2000 U.S. standard population and annual percent change (APC) were calculated using SEER* Stat v7.0.4. and Joinpoint analysis.

Results: AIR varied in the last 30 years between PreM and PostM and among races. Caucasian experienced highest AIR while 'others' race group had lowest. Among PreM women, Caucasian's AIR first decreased (APC = -1.31) until 1980 and then rised until 1999 (APC = 0.75, $p < 0.05$). Blacks increased until 1992 (APC = 2.17, $p < 0.05$) and then decreased until 2008, 'others' race group increased steadily in these years. Among PostM, Caucasian significantly increased from 1978 until 2000, Blacks sharply increased (APC = 4.70, $p < 0.05$) until 1986 and slowly increased until 2008 (APC = 0.58, $p < 0.05$). Other races increased until 1997 (APC = 3.24, $p < 0.05$) and leveled off until 2008 (APC = -0.90).

Conclusion: Results show trends in AIR of BC varies among races and pre- and post-menopausal women. Identify factors of variation is key to improve BC health care of these patients.

PO03-01

PTEROSTILBENE-INDUCED AUTOPHAGY PROTECTS BREAST CANCER CELLS FROM GROWTH INHIBITION

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Background/Purpose: As a nature phytoalexin found in grapes, resveratrol has been proposed as a potential drug for cancer chemoprevention and treatment. However, its poor bioavailability limits its potential clinical application. Pterostilbene, the natural dimethylated analog of resveratrol with greater bioavailability, was confirmed to inhibit tumor growth both *in vivo* and *in vitro*, demonstrating its potential for further clinical application.

Methods: The effect of pterostilbene on cell growth was determined by MTT assay and flowcytometry. Electromicroscopy examination and Western blotting were used to evaluate the induction of autophagy. Expression of various genes were determined by Western blotting and real-time RT-PCR.

Results: Pterostilbene could markedly inhibit the growth of two independent breast cancer cell lines. Both apoptosis and cell cycle arrest as well as the inhibition of wnt singling was induced by pterostilbene. The dominant-active mutant of β-catenin could reverse the growth inhibitory effect of pterostilbene. Interestingly, pterostilbene induced autophagy and blockage of autophagy augmented pterostilbene-induced growth inhibition.

Conclusion: The inhibition of wnt signaling is important to the growth inhibitory effect of pterostilbene. Pterostilbene-induced autophagy protects cancer cells from growth inhibition, indicating that the combination of autophagy inhibitors with pterostilbene and other therapeutics such as endocrine drugs could serve as a new and promising strategy for the treatment of breast cancer cells.

PO03-04

BIOMARKERS AFFECTING METASTASIS AND SURVIVAL IN PAIRED TISSUES OF 107 PATIENTS WITH METASTATIC BREAST CANCER

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Background/Purpose: The chemokine, CXCL12, and its receptor, CXCR4, have been known to play important roles in metastasis of several kinds of carcinoma. In preclinical study, VEGF regulates both CXCR4 expression and invasiveness. Tumors with higher Ki67 and EGFR expression were more prone to recur or metastasis. CD44+/CD24- subpopulation of breast cancer cells has highly invasive properties and involves in early stage of metastasis.

Methods: Between 1995 and 2009, among patients with breast cancer who underwent breast cancer surgery during following up patients who developed distant metastasis were screened for availability of metastatic sites tissue for immunohistochemistry (IHC) analysis. We reviewed patients' medical records and assessed CXCR4, CXCL12, VEGF, Ki67, EGFR, PTEN, CD24 and CD44 by IHC in primary sites and metastatic sites of these 107 patients.

Results: The median age was 48 years (range, 26 to 70 years). Most tumors were invasive ductal carcinoma (IDC) (98/107, 91.6%) and more than 2 cm (78/107, 72.8%). Fifty-six patients were positive axillary lymph nodes (56/107, 52.3%). 103 patients were assessed for HER2 expression by IHC, 35 (35/107, 32.7%) patients showed HER2 expression. CXCR4 were significantly relevant to brain metastasis [OR 11.1 (CI 1.0-121.2), $p = 0.05$]. Molecular subtypes of breast cancer were not predictive for brain metastasis and lung metastasis. Estrogen Receptor (ER), Progesterone Receptor (PR) expression and good histologic grade of tumor tissues were correlated significantly with longer overall survival.

Conclusion: Higher CXCR4 in primary breast cancer sites was related to brain metastasis. ER, PR expression and good histological grade were favorable prognostic factors for survival in patients with breast cancers.

Poster Discussion

PO03-05

MICRORNA-200C INCREASED RADIOSENSITIVITY OF A HUMAN BREAST CANCER CELLS

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Background/Purpose: The microRNA-200 (miR-200) family is known to regulate PI3K and to play a crucial role in epithelial to mesenchymal transition via controlling cell migration and polarity. In this study, we evaluated the potential of targeting miRNA-200c for overcoming radio-resistance of breast cancer cells having activated HER-2/PI3K signaling pathway. We also try to elucidate diverse mechanism of radiosensitization by miR-200c.

Methods: SKBR-3 human breast cancer cells were transfected with pre-miR-200c or control pre-miRNA using siPORT NeoFX™ transfection agent. Real-time PCR was performed and the fold-change of miR-200c levels was calculated and normalized to a hsa-mir-423 loading control. Expression level of target protein was monitored by western blot and immunofluoresce staining. Radiation survival was measured by clonogenic assay. The effects of migration on SKBR-3 cells were measured by wound healing assay and invasion was detected by transwell system. The effect of tubular formation was determined by matrigel assay.

Results: Ectopic overexpression of miR-200c attenuated p-AKT and p-ERK expression and radiosensitized SKBR-3 breast cancer cells. Overexpression of miR-200c prolonged radiation-induced γH2AX foci formation and downregulation of DNA-PKcs. Increased expression of mature miR-200c also suppressed the angiogenesis as evidenced by tubular formation, invasion and migration and led to down-regulation of HIF-1α and VEGF expression.

Conclusion: Taken together, these findings suggest that miR-200c may be a useful therapeutic target for overcoming radio-resistance of human breast cancer cells having activated PI3K signaling pathway. Work supported by Nuclear R&D Program (BAERI# 2008-2001417) & Basic Science Research Program (#313-2007-2-E00381) from National Research Foundation to Kim IA.

PO03-06

CLINICOPATHOLOGICAL CHARACTERISTICS OF BASAL TYPE BREAST CANCER

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Background/Purpose: Triple negative breast cancer (TNBC) is defined by the lack of estrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) expression. Patients with TNBC derive no benefit from molecularly targeted treatments such as endocrine therapy or trastuzumab, because they lack the appropriate targets for these drugs. Triple negative cancer consists of two subtypes: basal like and non basal like. The purpose of our study is to distinguish the clinicopathological characteristics of the two subtypes.

Methods: Between 2004 and 2010, 367 patients with primary breast cancer were investigated retrospectively in this study and ER, PgR, and HER2 status were evaluated in all cases. Moreover, we classified TNBC with basal type and non-basal type, by immunohistochemical staining epidermal growth factor receptor (EGFR), CK5/6.

Results: Subtype derived by molecular classification in breast cancer is luminal A (61%), luminal B (10%), HER2 (14%), and TNBC (15%). As for pathological analysis, solid tubular adenocarcinoma, nuclear grade 3 in TNBC and is more than those in non-TNBC. Basal type (71%) of TNBC have more lymph node metastasis and show worse prognosis than non-basal type (29%). Basal type was also significantly associated with ki67 labeling index ($p = 0.0001$), p53 expression ($p = 0.047$). Patients with basal type showed shorter overall survival ($p = 0.023$) than patients with non basal type.

Conclusion: The classification with subtype of TNBC by EGFR, CK5/6 is very useful as prognostic factor. So, we must produce any adequate new strategy for basal type of TNBC.

Poster Discussion

PO03-07

AQUAPORIN-5 PLAYS A KEY ROLE IN PROLIFERATION AND MIGRATION OF HUMAN BREAST CANCER CELLS

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Background/Purpose: Water channel protein aquaporin (AQP) is a family of transmembrane protein for water transport. Recent studies revealed that AQPs are likely to play a role in the tumor progression and invasion. We aimed to immunolocalize AQP5 in the human breast cancer tissues and its role on the proliferation and migration of human breast cancer cells.

Methods: mRNA and protein expression of AQP5 in human breast cancer cell lines (MCF-7 and MDA-MB-231) were examined by RT-PCR and immunoblotting analysis. Immunohistochemistry of AQP5 was performed on the paraffin sections of human breast cancer tissues. AQP5-knockdown in MCF-7 cells was induced by lentiviral shRNA-mediated gene silencing. Cell proliferation of breast cancer cells was examined by BrdU incorporation assay and modified Boyden chamber migration assay.

Results: RT-PCR and immunoblotting analysis revealed the expression of AQP5 mRNA and protein in human breast cancer cells and immunohistochemistry demonstrated AQP5 expression in the ductal epithelia of human breast tissues. Increased labeling intensity and loss of subcellular polarity of AQP5 expression in ductal epithelia were observed when the human breast cancer cells were becoming more progressive and invasive. Lentivirus-mediated AQP5-shRNA transduction or hyperosmotic stress induced by sorbitol treatment (100 mM for 24 hr) in MCF-7 cells resulted in the significant reduction of AQP5 expression, which was associated with markedly reduced cell proliferation and migration in MCF-7 cells.

Conclusion: The results demonstrate that AQP5 plays a role in the proliferation and metastasis of human breast cancer cells.

PO03-08

EFFECT OF SUPPLEMENTATION OF TANSHINONE IIA AND SODIUM TANSHINONE IIA SULFONATE ON THE ANTI-CANCER EFFECT OF EPIRUBICIN - AN IN VITRO STUDY

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Background/Purpose: Tanshinone IIA (Tan IIA) and sodium tanshinone IIA sulfonate (STS) were found to have protective effects on cardiomyocyte against adriamycin-induced damage, and may be used clinically. It is unclear whether the supplementation of STS or Tan IIA would affect the anti-cancer activity of anthracycline.

Methods: To evaluate the effect of Tan IIA or STS on the anti-cancer activity of epirubicin, an in vitro cell line study was performed using the BT-20 breast cancer cell line. The cell viability, apoptosis, Akt expression and uptake of epirubicin after supplementation of Tan IIA or STS in the epirubicin-treated BT-20 cells were measured and compared.

Results: Tan IIA inhibited BT-20 cell growth and induced apoptosis in a time- and dose-dependent manner. When Tan IIA was used with epirubicin, an increase of BT-20 cell apoptosis was accompanied with the decreasing phosphorylation of Akt. STS had no effect on the cell viability of BT-20 cells. However, when used with epirubicin, STS decreased the epirubicin-induced cytotoxicity and apoptosis in BT-20 cells (Fig. 1). The antagonistic effect of STS on epirubicin-induced cytotoxicity in BT-20 cells occurred concomitantly with the reduced epirubicin uptake and the increased phosphorylation of Akt. STS decreased the uptake of epirubicin in BT-20 cells and blocked epirubicin-induced apoptosis through activation of Akt (Fig. 2).

Conclusion: STS may interfered with the anti-cancer effect of epirubicin through the decrease uptake of epirubicin and activation of Akt. Meanwhile, Tan IIA may potentiate the cytotoxicity of epirubicin when used together.

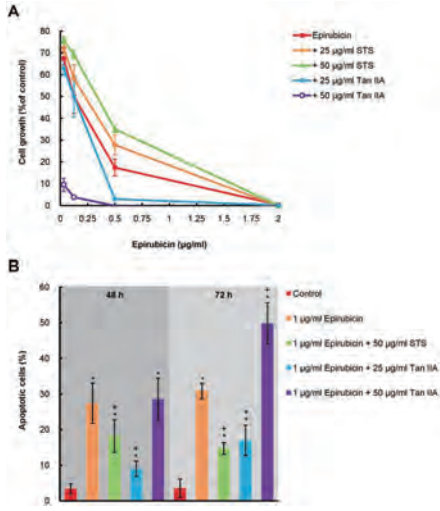
A
Cell growth (% of control)
Epirubicin (μg/ml)
Epirubicin
+ 25 μg/ml STS
+ 50 μg/ml STS
+ 25 μg/ml Tan IIA
+ 50 μg/ml Tan IIA
B
Apoptotic cells (%)
48 h
72 h
Control
1 μg/ml Epirubicin
1 μg/ml Epirubicin + 50 μg/ml STS
1 μg/ml Epirubicin + 25 μg/ml Tan IIA
1 μg/ml Epirubicin + 50 μg/ml Tan IIA

Fig. 1

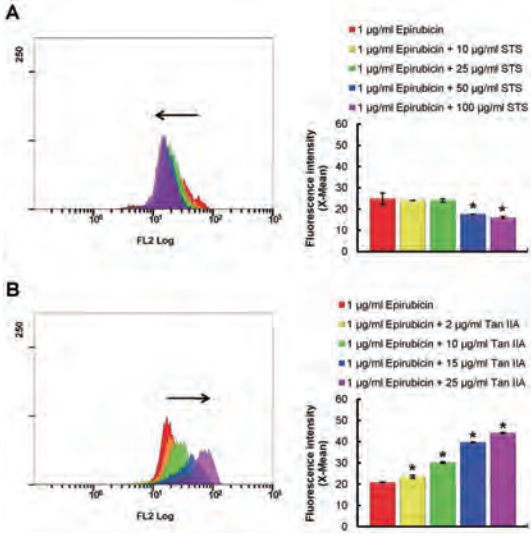
A
FL2 Log
1 μg/ml Epirubicin
1 μg/ml Epirubicin + 10 μg/ml STS
1 μg/ml Epirubicin + 25 μg/ml STS
1 μg/ml Epirubicin + 50 μg/ml STS
1 μg/ml Epirubicin + 100 μg/ml STS
Fluorescence intensity (X-Mean)
B
FL2 Log
1 μg/ml Epirubicin
1 μg/ml Epirubicin + 2 μg/ml Tan IIA
1 μg/ml Epirubicin + 10 μg/ml Tan IIA
1 μg/ml Epirubicin + 15 μg/ml Tan IIA
1 μg/ml Epirubicin + 25 μg/ml Tan IIA
Fluorescence intensity (X-Mean)

Fig. 2

PO03-09

DEATH AND RECURRENCE RATES OF THE PATIENTS WITH BREAST CANCER BY RESIDENTIAL DIFFERENT SOLAR IRRADIANCE BASED ON HR AND HER-2

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Background/Purpose: Vitamine D is a protective factor of breast cancer. Focusing on solar irradiance induced Vitamine D, we aimed to grasp the difference of the death and recurrence rates of the patients with breast cancer according to residential areas with different solar irradiance.

Methods: The subjects for this study were 11,425 patients who operated and were diagnosed with breast cancers in Asan Medical Center, Seoul, Korea from July 1989 to March 2010. The areas with relatively low solar irradiance was designated as the 1st group, those with the highest solar irradiance as the 3rd group, and others as the 2nd group. Also the patients were divided again into 4 subgroups according to HR and Her-2, with the death rate of the patients with breast cancer compared by the solar irradiance difference of each area. Collected data was analyzed with the crosstabs of IBM SPSS 19.0 Korean version.

Results: The death rates and the recurrence rates of the 3rd group was statistically significant less than that of the 1st group. The death rate of all subgroups of the 3rd group was statistically significant less than that of the 1st group. Except the Luminal B, the recurrence rate of other subgroups in the 3rd group was statistically significant less than that of the 1st group.

Conclusion: This study has an significant implication in that it shows the distribution of the death and recurrence rates of the patients with breast cancer according to the solar irradiance differences based on the HR and Her-2 reaction.

PO03-10

FASN INHIBITION BY AMENTOFLAVONE SUPPRESSES HER2 ONCOGENE IN SKBR3 CELLS

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Background/Purpose: Fatty acid synthase (FASN) is a potential therapeutic target for treatment of cancer and obesity, and is highly elevated in 30% of HER2-overexpressing breast cancers. A molecular link between FASN and the HER2 oncogene is a marker for poor prognosis in breast cancers. Considerable interest has developed in searching for novel FASN inhibitors as therapeutic agents in treatment of HER2-overexpressing breast cancers.

Methods: Two breast cancer cell lines were cultured using standard techniques. Cells were treated with increasing concentrations of amentoflavone. Apoptosis was determined by flow cytometry, and transcriptional regulation was determined by RT-PCR. Western blot analysis was performed to determine the effects of amentoflavone on FASN, the proteins involved in apoptosis, and HER2 related signaling proteins.

Results: Pharmacological inhibition of FASN by amentoflavone specifically down-regulated HER2 protein and mRNA, and caused an up-regulation of PEA3, a transcriptional repressor of HER2. In addition, pharmacological blockade of FASN by amentoflavone preferentially decreased cell viability and induced cell death in SKBR3 cells. Palmitate reduced the cytotoxic effect of amentoflavone, as the percentage of viable cells was increased after the addition of exogenous palmitate. Amentoflavone-induced FASN inhibition inhibited the translocation of SREBP-1 in SKBR3 cells. Amentoflavone inhibited phosphorylation of AKT, mTOR, and JNK. The use of pharmacological inhibitors revealed that the modulation of AKT, mTOR, and JNK phosphorylation required synergistic amentoflavone-induced FASN inhibition and HER2 activation in SKBR3 cells.

Conclusion: These results suggest that amentoflavone modulated FASN expression by regulation of HER2-pathways, and induced cell death to enhance chemopreventive or chemotherapeutic activity in HER2-positive breast cancers.

PO03-12

CARBOXYL-TERMINAL MODULATOR PROTEIN PROMOTES TUMORIGENESIS OF BREAST CANCER BY ENHANCING AKT/PKB ACTIVATION

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Background/Purpose: Carboxyl-terminal modulator protein (CTMP) was first identified as an Akt binding protein. Although the Akt binding domain of CTMP is still unknown, it has been demonstrated that CTMP regulates Akt activity through binding to the carboxyl-terminus of Akt at plasma membrane. However, contradict results of positive and negative effects of CTMP on Akt activation were reported recently. Thus, it is important to understand the role of CTMP on Akt activation and tumor malignancy.

Methods: The correlation of CTMP expression and Akt phosphorylation was analyzed using immunohistochemistry in breast cancer cell lines and clinical specimens. The tumorigenetic role of CTMP was evaluated by gain and loss of function approaches. The protein-protein interaction between CTMP and Akt was determined by immunoprecipitation, GST pull-down assay, and *in situ* proximity ligation assay.

Results: CTMP expression was upregulated and showed positive correlation with Akt phosphorylation in tumor specimens and malignant breast cancer cell lines. Stable overexpression of CTMP in MCF-7 cells promoted their cell proliferation as well as in vitro and in vivo tumorigenesis abilities. In contrast, knockdown of CTMP by siRNA significantly decreased the proliferation and in vitro invasion ability of MDA-MB-231 cells. We identified the N-terminal domain, containing 1-64 amino acids, of CTMP was responsible for CTMP binding to Akt. In addition, transient or stable overexpression of CTMP increased the sensitivity of insulin-induced Akt phosphorylation at both Thr308 and Ser473, which is primarily mediated by the PI3-kinase/Akt pathway.

Conclusion: we conclude that CTMP promotes Akt posphorylation and functions as an oncogenic molecule in human breast cancer.

Poster Discussion

PO03-13

IL-21 ENHANCES CYTOTOXICITY OF *EX VIVO* EXPANDED NK CELLS AGAINST BREAST CANCER CELLS

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Background/Purpose: The expanded NK cells have an ability to kill tumor target by direct cytotoxitiy and by antibody-dependent cellular cytotoxicity (ADCC). Interleukin-21, one of promising cytokines with anti-tumor activity, stimulates cytotoxicity and IFN-γ production in NK cells. In this study, we examined cytotoxicity of *ex vivo* expanded NK cells stimulated with IL-21 against breast cancer

Methods: To activate and expand NK cells, PBMC were isolated from healthy donors and co-cultured with 100 Gy gamma-ray irradiated K562-mb15-41BBL cells expressing 4-1BB ligand and membrane-bound IL-15 in the presence of IL-2 and IL-15 for 3 weeks. After 4 day-stimulation of IL-21, cytotoxicity was measured using WST-1 at 1:1, 2:1, and 4:1 effector-to-target (E/T) ratios for 4 hours in the absence and presence of 100 ng/mL trastuzumab.

Results: Cytotoxicity of expanded NK cells against MCF-7, SKBR3, and T47D was 38.3%, 32.7%, and 52.5% at 1:1 E/T ratio, 67.1%, 54.2%, 72.1% at 2:1 E/T ratio, and 86.9%, 71.7%, 91.9% at 4:1 E/T ratio, respectively. Cytotoxicity of expanded NK cells significantly increased against trastuzumab coated SKBR3 than the uncoated ($p < 0.05$). Cytotoxicity of expanded NK cells stimulated with IL-21 significantly increased against MCF-7, SKBR3, and T47D cell lines than without IL-21 stimulation ($p < 0.05$), while the cytotoxicity did not significantly increase in response to trastuzumab-coated the cell lines.

Conclusion: Expanded NK cells showed high cytotoxicity by direct cytotoxicity and by ADCC even at the lower E/T ratio. IL-21 significantly enhanced cytolytic activity of expanded NK cells against breast cancer cells by mainly direct cytotoxicity, while it has a minimal effect on ADCC.

PO03-14

COMPARATIVE ANALYSIS OF HORMONE RECEPTOR STATUS AND HER-2 EXPRESSION BETWEEN PRIMARY AND RECURRENT BREAST CANCER

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Background/Purpose: Recent retrospective reviews suggest that the estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor type 2 (HER2) receptor may differ between the primary and recurrence or distant metastases. In these reports, the rate of discordance for ER, PR and HER2 status ranged between 10 and 30%.

Methods: Primary and recurrent tumors from 42 patients with recurrent breast cancer were studied. ER, PR, and HER2 statu were determined by immunohistochemistry and/or fluorescent *in situ* hybridization.

Results: The sites of biopsied recurrent/metastatic lesions are regional soft tissue (21.4%), lymph nodes (30.1%), lung (26.1%), bone (16.6%), brain (4.8%), and ovary (2.4%). Discordance for ER was 11% (n = 5). Among these, 7.1% (n = 3) patients had ER-positive primary tumor but ER-negative metastasis and 4.8% (n = 2) had ER-negative primary but ER-positive metastasis. Discordance for ER was 19% (n = 8). Among these, 14.3% (n = 6) had PR-positive primary but PR-negative metastasis and 4.8% (n = 2) had PR-negative primary and PR-positive metastasis. HER-2 status was known in both primary tumor and metastasis in 34 patients. Among these patients, 15.9% (n = 2) had discordant results. Among these discordant cases, two had negative primaries and positive metastasis and no cases had positive primaries and negative metastasis.

Conclusion: As these discordant results make changes in treatment decision, a biopsy of the metastatic lesion could be recommended in patients with metastatic breast cancer.

PO03-15

PROGNOSTIC SIGNIFICANCE OF P53 IN DUCTAL CARCINOMA *IN SITU*

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Background/Purpose: Gene alteration of p53 accounts for one of the most common genetic events in human tumors, and more than 50% of malignant tumors contain p53 abnormalities. Serum appearance of anti-p53 antibodies often coexists with p53 gene mutations, and its significance as an indicator of aggressive behavior of tumors and/or worse prognosis of human patients with tumors was the predominant suggestion arising from a panel of investigations. We investigated the prognostic significance of p53 in Ductal carcinoma *in situ*.

Methods: We analyzed 137 patients with Ductal carcinoma *in situ* who underwent surgery at our institution between 2001 and 2006. We subclassified the DCIS into p53 phenotype and non-p53 phenotype. We used cross table as analyzing methods in clinicopathologic factors distribution between two groups.

Results: A total of 40 (29.2%) cases were positive for p53, and bcl-2 expression was significantly associated with lower grade, expression of hormone receptor positivity. In a univariate analysis, p53 expression remained a significant predictor of recurrence in patients with DCIS ($p = 0.033$).

Conclusion: p53 expression was a poor prognosticator in patients with DCIS.

PO03-16

PROGNOSTIC SIGNIFICANCE OF BCL-2 IN TRIPLE NEGATIVE BREAST CANCERS

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Background/Purpose: B-cell lymphoma (Bcl)-2 is an anti-apoptotic gene, and it is a poor prognostic factor in various malignant tumors. However, the prognostic significance of bcl-2 expression in breast cancer remains controversial. We investigated the prognostic significance of bcl-2 in triple negative breast cancers.

Methods: We analyzed 175 patients with triple negative breast cancer who underwent surgery at our institution between 2001 and 2006. We subclassified the triple negative breast cancers (TNBC) into Bcl-2 phenotype and non Bcl-2 phenotype. We used cross table as analyzing methods in clinicopathologic factors distribution between two groups

Results: A total of 101 (57.0%) cases were positive for Bcl-2, and Bcl-2 expression was significantly associated with earlier stage, lower grade, expression of hormone receptor positivity. In a univariate analysis, Bcl-2 expression remained a significant predictor of recurrence in patients with TNBC ($p = 0.013$).

Conclusion: Bcl-2 expression was a poor prognosticator in patients with the triple-negative subtype.

PO03-17

AROMATASE INHIBITOR INCREASES LET-7F WHICH TARGETS CYP19A1 IN HUMAN BREAST CANCER

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Background/Purpose: Aromatase inhibitors (AIs) are considered gold standard of endocrine therapy for estrogen receptor positive postmenopausal breast carcinoma patients. AI treatment gives rise to global changes in genetic profile including aromatase mRNA itself but its detailed molecular mechanisms have not been fully elucidated. The purpose of this study was to identify microRNA (miRNA) expression alterations by letrzole treatment and to explore the possible targets of those miRNAs.

Methods: We profiled miRNA expression before and after treatment with letrozole in MCF-7 co-cultured with intratumoral stromal cells using miRNA PCR array. To determine target genes of miRNAs, we used multiple target scan algorithms. mRNA and protein expression of target genes in breast carcinoma tissues were confirmed by real time PCR and immunohistochemistry, respectively. A 3'UTR luciferase assay was performed to verify putative target genes. Cell proliferation assay and wound healing assay were carried out for functional analysis of miRNA.

Results: Global alterations of miRNA expression profiles by letrozole treatment were observed. Of note, expression of let-7f was up-regulated by letrozole which computational analysis predicted let-7f to directly target aromatase gene (CYP19A1). Letrozole decreases aromatase mRNA in MCF-7 cells. Also, high aromatase mRNA and protein expressions were related with low let-7f expression in breast carcinoma tissues. Let-7f transfection significantly decreased 3'UTR luciferase activity of CYP19A1 and inhibits cell proliferation/migration in MCF-7

Conclusion: Let-7f, a tumor suppressor miRNA in breast carcinoma, directly targets CYP19A1 and is restored by AI treatment. Therefore, we may postulate that via let-7f, AI down-regulates aromatase mRNA and moreover exhibits tumor-suppressing effects on breast carcinoma.

PO03-18

COLLAGEN GEL DROPLET EMBEDDED CULTURE-DRUG SENSITIVITY TEST AND KI67 EXPRESSION IN ESTROGEN RECEPTOR-POSITIVE BREAST CANCER

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Background/Purpose: In general, the efficiency of chemotherapy is lower in patients with estrogen receptor (ER)-positive breast cancer as compared with those with ER-negative one. Collagen gel droplet embedded culture-drug sensitivity test (CD-DST) is the newly developed in vitro chemosensitivity test that has several advantages over the conventional ones. The Ki67 has shown strong prognostic effects and been also predictive of greater response to most chemotherapies. The aim of present study is to examine the correlation between Ki67 and CD-DST for the efficacy of anthracyclines and taxanes in patients with ER-positive and HER2 negative breast cancer.

Methods: CD-DST test was performed in 63 patients with ER-positive and HER2-negative breast cancer during the period from August 2001 to November 2006. The resected breast cancer specimens at the surgery were used for CD-DST and immunohistological examination of Ki67.

Results: Four anticancer drugs [adriamycin (ADM), epirubicin (EPI), Docetaxel (DOC), paclitaxel (PTX)] were estimated for CD-DST. In CD-DST, the chemosensitivity to each anticancer drug were as follows: ADM 20.4%, EPI 67.3%, DOC 66.7%, PTX 43.6%. Ki67 were significantly higher in the sensitive group than the resistant group to DOC ($p = 0.021$) and, to PTX ($p = 0.033$). In addition, We observed a significant correlation between Ki67 LI over 30% and the chomosensitivity to PTX.

Conclusion: CD-DST and Ki67 can identify a subset of patients with ER-positive and HER2-negative breast cancer who could be sensitive to chemotherapy, particularly taxnes therapy.

Poster Discussion

PO03-19

COMPUTATIONAL STUDY OF ESTROGEN RECEPTOR-ALPHA ANTAGONIST WITH THREE-DIMENSIONAL QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP, SUPPORT VECTOR REGRESSION, AND LINEAR REGRESSION METHODS

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Background/Purpose: Human estrogen receptor (ER) isoforms, ERα and ERβ, have long been an important focus in the field of biology. To better understand the structural features associated with the binding of ERα ligands to ERα and modulate their function, several qantitative structure-activity relationship (QSAR) models, including CoMFA, CoMSIA, SVR, and LR methods, have been employed to predict the inhibitory activity of 68 raloxifene derivatives.

Methods: QSAR modeling was used.

Results: In the SVR and LR modeling, 11 descriptors were selected through feature ranking and sequential feature addition/deletion to generate equations to predict the inhibitory activity toward ERα. Among four descriptors that constantly appear in various generated equations, two agree with CoMFA and CoMSIA steric fields and another two can be correlated to a calculated electrostatic potential of ERα.

Conclusion: Together, all the four models are in agreement with each other. Furthermore, these models are helpful in constructing better inhibitors based on the core of raloxifene.

PO04-01

IMPACT OF CHEMOTHERAPY-INDUCED AMENORRHEA ON RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Background/Purpose: Although chemotherapy and ovarian ablation independently improve the outcome of breast cancer, there is controversy about the benefit of chemotherapy-induced amenorrhea (CIA) in breast cancer. We investigated impact of CIA on response to neoadjuvant chemotherapy in breast cancer patients.

Methods: We reviewed the records of 198 premenopausal patients with breast cancer treated with neoadjuvant chemotherapy between January 2005 and December 2010. CIA defined as serum FSH level ≥ 40 IU/L after completion of all scheduled neoadjuvant chemotherapy and prior to definitive surgery.

Results: Among 198 breast cancer patients, 132 patients (66.7%) developed CIA after neoadjuvant chemotherapy. 156 patients (78%) underwent Docetaxel and Adriamycin (DA) chemotherapy. The age of CIA patients was older than non-CIA patients (41.55 ± 5.55 years vs. 38.27 ± 6.86 years, p = 0.001). The incidence of CIA after neoadjuvant chemotherapy was significantly higher in responder group (responder vs. nonresponder: 87 patients (74.4%) vs. 45 patients (55.6%); p = 0.006). Additionally, FSH level after all scheduled neoadjuvant chemotherapy was significantly higher in responder group (56.41 ± 32.41 IU/L vs. 45.76 ± 30.31 IU/L; p = 0.021). In univariate analysis, CIA (p = 0.006) and total number of chemotherapy cycle regardless of chemotherapy regimen (p = 0.04) were significantly associated with tumor response. CIA was only independent factor for tumor response after neoadjuvant chemotherapy on multivariate analysis (p = 0.012).

Conclusion: CIA after neoadjuvant chemotherapy was significantly associated with response to neoadjuvant chemotherapy in locally advanced breast cancer.

PO04-02

PROGNOSTIC FACTORS AFFECTING SURVIVAL OF BREAST CANCER PATIENT WITH BONE ONLY METASTASIS

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Background/Purpose: Bone only metastasis patients have distinguished features and clinical course compared to other distant mestasis patients. We explored this study to clarify the relationship of the survival of the patients with breast cancer and bone metastasis.

Methods: From January 1991 to June 2011, 3,160 of breast cancer patients were treated at Gangnam Severance hospital, Seoul, Korea. Among them, patients who developed bone metastasis during follow up period after treatment of breast cancer and patients diagnosed as primary breast cancer with bone only metastasis at initial diagnosis were included in this study. We retrospectively collected the clinico-pathologic data. We analyzed the relationship between the clinico-patholgic factors and the survival after bone metastasis.

Results: One hundred fourteen patients with breast cancer and bone only metastasis were identified from the database of Ganganam Severance hospital. Of these patients, 89 (78.0%) had bone only recurrence after radical surgery and 25 (22.0%) showed bone metastatasis at initial diagnosis. In the bone only recurrence group, median age of selected patients was 43.0 years old, median follow-up period was 69.6 months, and median survival after bone metastasis was 26.5 months. In the survival analysis for bone only recurrence group, positive hormone receptor ($p = 0.028$), small number of metastaic lymph node ($p = 0.039$), bisphosphonate treatment ($p = 0.006$), and solitary bone metastasis ($p = 0.033$) was identified to be prognostic factors for better survival after bone metastasis.

Conclusion: Positivity of hormone receptor and negativity of lymph node status were associated with better outcomes. Furthermore, bisphosphonate administration could be considered in the treatment for the patients with bone metastasis.

PO04-03

CLINICAL EVALUATION OF NIPPLE-SPARING MASTECTOMY AND IMMEDIATE BREAST RECONSTRUCTION WITH IMPLANT; 25 CASES

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Background/Purpose: Operation method for breast cancer has been changed since radical mastectomy period. Recently, breast conserving operation and oncoplastic surgery are popular because early breast cancer rate increased. Patients also are satisfied with conventional conserving surgery and oncoplastic surgery .

Methods: From June 2009 till June 2011, twenty five patients who underwent nipple sparing subcutaneous mastectomy with immediate implant-based breast reconstruction were analyzed. implant material was saline or cohesive silicone bag. All patients were received chemotherapy or hormonal therapy. The women were followed for complications until June 2011

Results: Twenty five patients underwent nipple sparing mastectomy and immediate breast reconstruction during the study period, with a mean postoperative follow-up of 9.76 months. ALL patients had expander/implant reconstruction. three patients received neoadjuvant chemotherapy and 17 patients received postoperative chemotherapy but four patients were received only tamoxifen. Twenty one patients were received radiotherapy. Four ductal carcinoma *in situ* (DCIS) patients did not received radiotherapy. Patient satisfaction was assessed and they had similar general and aesthetic satisfaction scores. Complications occurred in seven patients (28%). There was five episode (20%) of postoperative infection resulting in implant loss, one episode (4%) of seroma. One episode of bleeding (4%) there was no complication after radiotherapy.

Conclusion: Immediate implant-based breast reconstruction is a safe and viable option that can provide a very good aesthetic result in appropriately selected candidates. The technique is aesthetically superior to delayed reconstruction and is associated with high levels of patient satisfaction and breast sensitivity and a low rate of morbidity.

Table 1. Comparison of cavity (CM) and lumpectomy (LM) margin statuses at the case level.

Lumpectomy margin	Cavity margin		P	Positivity rate for CMs %	Positivity rate for LMs %
	Positive	Negative			
Positive	10	10	<0.001†	30.1	12.3
Negative	40	103			
Subgroup analysis					
Subgroup of patients receiving neoadjuvant chemotherapy					
Positive	4	0	<0.001†	47.2§	11.1¥
Negative	14	18			
Subgroup of patients that did not receive neoadjuvant chemotherapy					
Positive	6	10	0.011†	25.2	12.6
Negative	26	85			

* McNemer's test for categorical variables was applied. § Chi-squared test was applied between the NST subgroup and the non-NST subgroup to compare the CM positivity rate. P = 0.012. ¥ Chi-squared test was applied between the NST subgroup and the non-NST subgroup to compare the LM positivity rate. P > 0.05.

Table 1.

Table 2. Comparison of cavity (CM) and lumpectomy (LM) margin status at the individual margin level†

Margin assessment methods	Positive		Negative		Total	P
	No.	%	No.	%		
CM	115	8.0	1332	92.1	1447	<0.001
LM	38	1.8	2022	98.2	2060	
Subgroup analysis						
Subgroup of patients receiving neoadjuvant chemotherapy						
CM	53	15.5§	288	84.5	341	<0.001‡
LM	19	4.2¥	437	95.8	456	
Subgroup of patients that did not receive neoadjuvant chemotherapy						
CM	62	5.6	1044	94.4	1106	<0.001‡
LM	19	1.2	1585	98.8	1604	

† In total, 1,447 cavity margins and 2,060 lumpectomy margins were obtained from 163 patients. CMs, cavity margins; LMs, lumpectomy margins.
‡ Chi-squared test was performed between the NST subgroup and the non-NST subgroup. § Chi-squared test was applied between the NST subgroup and the non-NST subgroup to compare the CM positivity rate. P < 0.001. ¥ Chi-squared test was applied between the NST subgroup and the non-NST subgroup to compare the LM positivity rate. P < 0.001.

Table 2.

Table 3. Multivariate analysis: clinicopathological features correlated with positive margin

	HR	95% CI	P-value
Cavity margin			
Delivery of NST	2.63	1.07-6.46	0.036
Axillary lymph node involvement	3.92	1.71-9.03	0.001
Histological subtype			<0.001
Presence of DCIS versus IDC without DCIS	11.17	3.68-33.89	<0.001
Other pathological subtypes versus IDC without DCIS		NS	
Lumpectomy margin			
Age (>50 years versus. ≤50 years)	0.209	0.06-0.70	0.011

DCIS, Ductal carcinoma in situ; IDC, Invasive ductal carcinoma

Table 3.

PO04-04

LOCALLY ADVANCED BREAST CANCER EFFECTIVELY TREATED WITH HELICAL TOMOTHERAPY AND ENDOCRINE THERAPY

Jihye Cha[1], Seung Il Kim[2], Byeong Woo Park[2], Joohyuk Sohn[3], Chang-ok Suh

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[3]*Department of Internal Medicine, Yonsei Univ. Health System, Korea*

Background/Purpose: To report the treatment outcome of unresectable locally advanced breast cancer with helical tomotherapy and aromatase inhibitor.

Methods: In December 2009, a 69-year-old female presented to breast surgeon with a ulcerative mass larger than 10 cm on her left breast. She was diagnosed as inoperable, cT4N2M1. She showed sternal metastasis (Figure 1). She began systemic endocrine therapy with aromatase inhibitor. After one month of endocrine therapy, she received total 62.5 Gy to primary mass, metastatic axillary nodes and sternal metastasis, 55 Gy to left whole breast, axilla and supraclavicular area by helical tomotherapy using simultaneous boost technique.

Results: Primary mass was markedly regressed after radiotherapy. It showed further regression after radiotherapy for 6 months. Radiation dermatitis was recovered within a month after the radiotherapy. Imaging studies including positron emission tomography? computed tomography confirmed favorable treatment response; the extensive skin enhancement and thicken was decrease in the extent and metabolism as well as metastatic axillary lymph nodes and the sternal metastasis was disappeared (Figure 2). In October 2010, she underwent left modified radical mastectomy and tension free skin closure with latissimus dorsi flap. Pathology results showed residual invasive ductal carcinoma of 0.3 cm size and no residual axillary lymph node metastasis. She is still being treated with aromatase inhibitor after the surgery and her disease status is no evidence of disease.

Conclusion: Locally advanced, widely skin invading inoperable breast cancer can be effectively managed by endocrine therapy and aggressive local radiotherapy by helical tomotherapy.

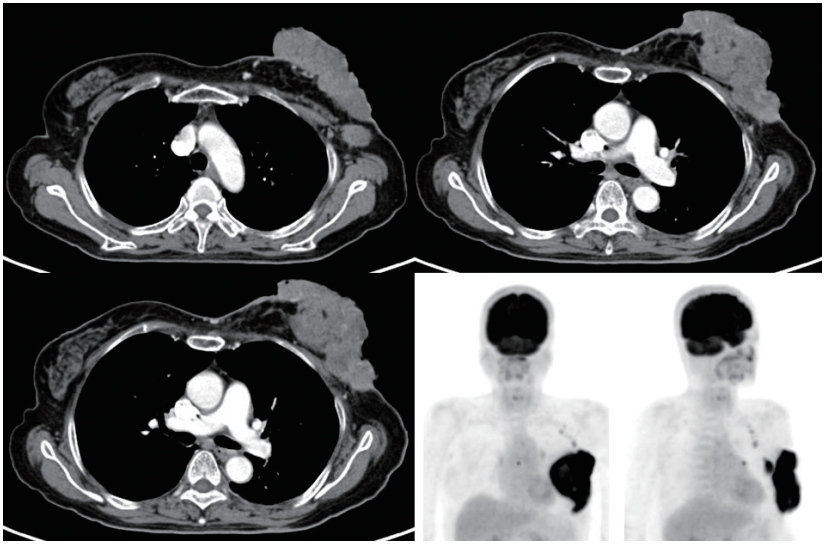

Figure 1.

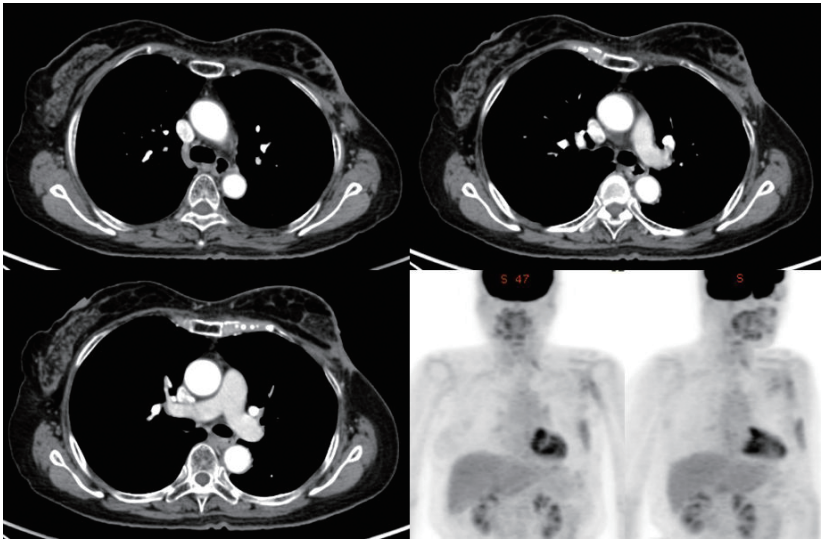

Figure 2.

PO04-07

THE EFFICACY OF ARM NODE PRESERVING SURGERY USING AXILLARY REVERSE MAPPING FOR PREVENTING LYMPHEDEMA IN PATIENTS WITH BREAST CANCER

Yu Jeong Seo, Mi Jin Hwang, Gi Tak Son, Je Hyeong Lee, Jung Eun Choi, Su Hwan Kang, Soo Jung Lee

Department of Breast Endocrine Surgery, Yeungnam Univ. Hospital, Korea

Background/Purpose: Axillary reverse mapping technique to identify and preserve arm node during SLNB or ALND developed to prevent lymphedema. The purpose of this study was to evaluate the short term incidence of lymphedema after arm node preserving surgery.

Methods: From January 2009 to October 2010, 97 breast cancer patients who underwent ARM were enrolled. 2.5 mL blue-dye was injected in ipsilateral-upper-inner arm. After at least 20 minutes after injection, SLNB or ALND was performed and blue stained arm nodes were identified. Patients were divided into two groups, arm node preserved group (70 in ALND, 10 in SLNB) and unpreserved group (13 in ALND, 4 in SLNB). The difference of arm circumference between preoperative and postoperative was checked in these groups.

Results: The mean number of identified blue stained arm nodes was 1.4 ± 0.6. In the majority of patients (92%), arm nodes were located between the lower level of the axillary vein and just below the second intercostobrachial nerve. In arm node unpreserved group, 2 patients had metastasis in their arm node. Among ALND patients, in arm node preserved group, the difference of arm circumference between preoperative and postoperative in ipsilateral and contralateral arm was 0.27 cm and 0.07 cm, respectively, whereas 0.47 cm and -0.03 cm in unpreserved group, and one lymphedema was found. No difference was found between arm node preserved and unpreserved group among SLNB patients.

Conclusion: Arm node preserving was possible in all breast cancer patients with identifiable arm node, except for those with high surgical N stage, and lymphedema did not develop in patient with arm node preserving surgery.

PO04-08

PATTERNS OF ANXIETY AND DEPRESSION DURING BREAST CANCER TREATMENTS: A PROSPECTIVE STUDY

Eun-kyung Choi[1], Im-ryung Kim[1], Seok-jin Nam[2], Jeong Eon Lee[2], Se-kyung Lee[2], Jung-hyun Yang[3], Dong-young Noh[4], Wonshik Han[4], Juhee Cho[1]

[1]*Cancer Education Center, Samsung Comprehensive Cancer Center, Samsung Medical Center, Korea*
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[4]*Department of Surgery, Seoul National Univ. Hospital, Korea*

Background/Purpose: Anxiety and depression are the most common psychological disorders observed in breast cancer patients. This study aims to investigate the impact of breast cancer diagnosis and its treatment on anxiety and depression of patients with breast cancer over time.

Methods: Between July 2010 and December 2010, we recruited patients with non-metastatic breast cancer who were expected to receive breast cancer treatments (n = 411) from two cancer hospitals in Seoul, Korea. Study participants completed questionnaires on anxiety and depression, quality of life at enrollment, after surgery, during chemotherapy, and during radiotherapy. Anxiety and depression was measured using Hospital Anxiety and Depression Scale (HADS).

Results: The mean age of the participants was 46.4 (SD 7.91) year old. 44.9% and 37.6% of them had stage I and II breast cancer, respectively. 83.0% of the patients had lumpectomy, and 70.6% and 85.9% had chemotherapy and radiotherapy, respectively. There were 22.9% and 43.5% patients who had abnormal anxiety and depression respectively at baseline. While there was no significant change with depression, the proportion of abnormal anxiety rapidly decreased after surgery ($p < 0.01$). The patterns of anxiety and depression during breast cancer treatments described in Figure 1.

Conclusion: Breast cancer patients were more likely to have abnormal anxiety before surgery and depression throughout the treatment. They should be routinely screened for anxiety and depression once they are diagnosed with the disease. Clinical pathway and education programs also need to be developed for managing anxiety and depressive symptoms with timely manner.

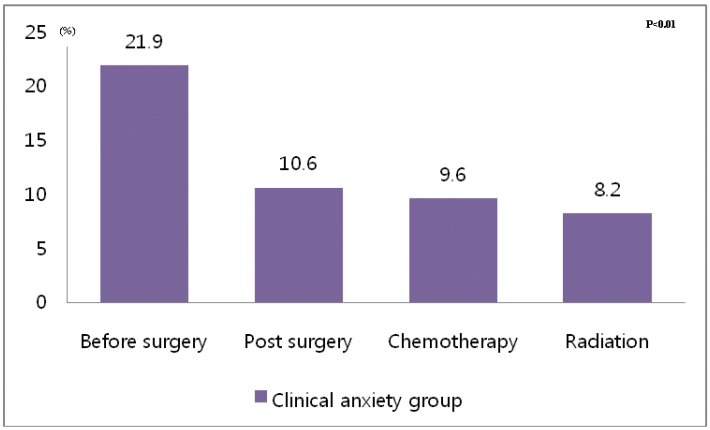
25
(%)
20
15
10
5
0
21.9
10.6
9.6
8.2
P<0.01
Before surgery
Post surgery
Chemotherapy
Radiation
Clinical anxiety group

Fig. 1

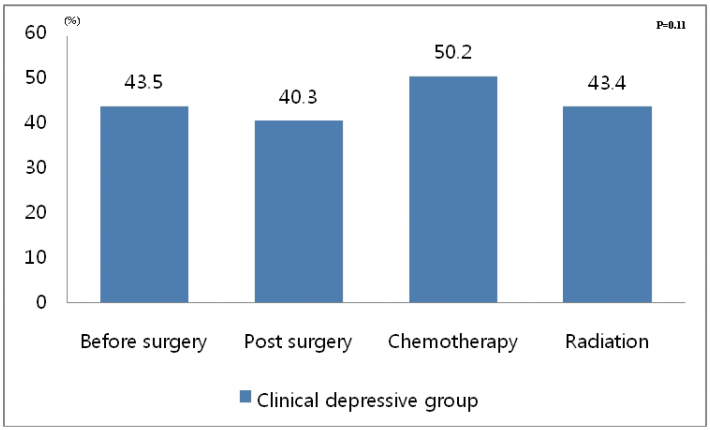
60
(%)
50
40
30
20
10
0
43.5
40.3
50.2
43.4
P=0.11
Before surgery
Post surgery
Chemotherapy
Radiation
Clinical depressive group

Fig. 2

PO04-10

DOSE-DENSE CHEMOTHERAPY IN HIGH-RISK BREAST CANCER PATIENTS: TREATMENT OUTCOME AND TOXICITY

Salah El Mesidy, Mohsen Mokhtar, Amr El-kashif, Loay Kasem

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Background/Purpose: To prospectively assess the treatment outcome of dose-dense adjuvant doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) in high-risk breast cancer patients (dose-dense arm) and to compare it with the available treatment results of the conventionally scheduled fluorouracil, doxorubicin, and cyclophosphamide (FAC) used to treat high-risk patients (historical control arm). Study endpoints included relapse-free survival (RFS), overall survival (OS) and toxicity.

Methods: After mastectomy or breast conservative surgery, high-risk node-positive breast cancer patients were assigned to receive adjuvant 4 cycles of doxorubicin/cyclophosphamide followed by 4 cycles of paclitaxel (AC/T) every 2 weeks. The treatment outcome of dose-dense AC/T was compared with that of the conventionally treated high-risk patients using adjuvant 6 cycles of FAC combination

Results: At a median follow up of 37 months (range 12-48 months), the 3-year adjusted RFS rates for AC/T and FAC were 76% and 54.6%, respectively ($p = 0.04$) and the mean disease-free interval was 40.6 ± 7.2 months (95% CI, 37.7-43.6) for dose-dense AC/T arm vs. 36.9 ± 6.9 months (95% CI, 32.3-41.5) for FAC arm ($p = 0.042$). The subgroup analysis revealed that dose-dense chemotherapy had a statistically significant positive effect on the 3-year RFS in premenopausal patients, patients with 10 or more (N3) positive axillary lymph nodes, positive ER status

Conclusion: Dose-dense AC/T significantly improved the relapse-free survival in patients with high-risk primary breast cancer and was less well tolerated compared with the conventionally scheduled FAC (historical control). The benefit was evident in premenopausal patients, extensive axillary nodal metastasis and positive ER status

PO04-11

THE FACTORS ASSOCIATED WITH RE-EXCISION AFTER BREAST-CONSERVING SURGERY FOR EARLY STAGE BREAST CANCER

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Background/Purpose: Re-excisions after breast conserving surgery (BCS) for breast cancer are causing delays in adjuvant treatment, associated morbidity, and poor aesthetic results. So, the effort to reduce the re-excision rate is essential. The aim of this study was to assess the re-excision rate and the factors associated with re-excision after BCS for early stage breast cancer.

Methods: We retrospectively reviewed the medical records of 671 patients who underwent BCS for early breast cancer at Seoul National University Bundang Hospital between June 2003 and February 2011. Univariate and Mutivariate analyses were performed to examine the clinicopathological factors related to positive margin status.

Results: Of the 671 patients, 66 (9.85%) required re-excision; 48 were BCS and 18 were total mastectomy. Of the 48 patient who underwent 2nd BCS, 11 (22.92%) required 2nd re-excision. Mean patient age was 51 years and BMI was 23.35. Mean age of no-re-excision group was relatively higher than that re-excision group (51.3 years vs. 48.3 years; $p = 0.041$). Palpable lesion was more often associated with re-excision than non-palpable lesion (12.0% vs. 6.3%; $p = 0.022$). Multifocal tumors (17.9% vs. 8.4%; $p = 0.003$) and presence of ductal carcinoma *in situ* (DCIS) (11.4% vs. 5.0%; $p = 0.017$) were also associated with re-excision.

Conclusion: In our institution, the rate of re-excision is low, even though intraoperative frozen section is not performed. Patients with non-palpable, multifocal tumors and DCIS component are more likely to have positive margin after BCS. These factors should be considered planning proper surgical management of early breast cancer.

PO04-12

UNFAVORABLE PROGNOSIS IN VERY YOUNG OVERWEIGHT PATIENTS (<35 YEARS) WITH EARLY STAGE HORMONE RECEPTOR POSITIVE BREAST CANCER

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[1]Breast Cancer Center, National Cancer Center, Korea
[2]Cancer Biostatistics Branch, National Cancer Center, Korea

Background/Purpose: We aimed to evaluate prognosis in young age receiving preoperative systemic chemotherapy (PSC).

Methods: We reviewed a total of 289 stage II/III breast cancer patients with PSC followed by surgery and adjuvant treatment between 2002 and 2006.

Results: Of thirty eight patients (13.1%) aged younger than 35 years, a pathologic complete response (pCR) was achieved in 2 (5.3%), 16 (42.1%) experienced recurrence and 11 (28.9%) died. On multivariable analysis, age < 35 years, clinical progressive disease, HER2 positivity without anti-HER2 therapy, and the axillary nodal non pCR were independent prognosticators. When clinical outcomes were analyzed with reference to age, body mass index (BMI) and hormone receptor status, younger patients in subgroups with hormone receptor positive disease (5-year DFS rate, 61.9% in < 35 years vs 82.1% in ≥ 35 years, $p = 0.04$; 5-year OS rate, 76.2% vs 93.9%, $p = 0.004$) and BMI ≥ 25.0 (5-year DFS rates; 45.5% vs 75.4%; $p = 0.01$, 5-year OS rates; 72.7% vs 86.4%; $p = 0.02$) had a particularly unfavorable prognosis.

Conclusion: Young breast cancer patients (< 35 years) in our series, particularly within an overweight subgroup having hormone receptor positive disease, had a significantly worse prognosis.

PO04-13

PREDICTIVE FACTORS FOR INVOLVEMENT OF AXILLARY LYMPH NODE IN POSITIVE SENTINEL NODE PATIENTS

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Background/Purpose: Recent results from the ACOSOG Z0011 showed that the role of axillary dissection for sentinel node positive breast cancer patients is questionable. Here, we studied the predictive factor for axillary node involvement in positive sentinel node patients.

Methods: Between January 2003 and May 2011, we performed 652 cases of sentinel node biopsy, and 168 cases had sentinel node metastasis by pathologic result. We divided into two groups according to non-sentinel lymph node (NSLN) metastases and reviewed their medical record retrospectively. Clinicopathological factors were compared including age, operation method, histologic type, histologic grade, nuclear grade, tumor size, T stage, lymphovascular invasion, multiplicity of tumor, preoperative radiologic finding of axillary node metastases, biologic marker such as estrogen receptor (ER), progesterone receptor (PR), c-erbB2, number of positive sentinel node, total harvested node, total harvested NSLN.

Results: Out of 168 patients, 79 (47%) patients had NSLN metastases and 89 (53%) patients did not. Between two groups, univariate analysis showed that patients who had breast conserving procedure (BCP) rather than mastectomy, negative lymphovascular invasion and negative finding at preoperative axillary imaging found to be associated with less likelihood of NSLN metastases. Multivariate analysis showed same result with statistical significance.

Conclusion: According to this study, sentinel lymph node biopsy alone can provide adequate treatment and staging in presence of such factors: BCP, negative lymphovascular invasion and negative preoperative axillary imaging despite of metastases on sentinel lymph nodes. More prospective randomized controlled trials supporting omission of axillary dissection are necessary.

PO04-15

INTERSTITIAL PNEUMONIA ASSOCIATED WITH NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

Hidemi Kawajiri[1], Tsutomu Takashima[1], Shinichiro Kashiwagi[1], Taeko Nakano[2], Yasuko Mitsukawa[3], Noriko Kawakami[1], Naoki Aomatsu[1], Naoyoshi Onoda[1], Tetsuro Ishikawa[1], Kosei Hirakawa[1]

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[2]*Department of Nursing, Osaka City Univ. Hospital, Japan*
[3]*Department of Pharmacy, Osaka City Univ. Hospital, Japan*

Background/Purpose: Although infrequently encountered, interstitial pneumonia (IP) is one of the major adverse events during chemotherapy. In particular for the patient on neoadjuvant chemotherapy (NAC), scheduled future treatment plan should critically be interfered by the occurrence of IP. We experienced five cases of breast cancer that were discontinued NAC by the chemical pneumonia.

Methods: Among 95 women with locally advanced breast cancer who had been administered FEC100 (fluorouracil 500 mg/m^2, epirubicin 100 mg/m^2 and cyclophosphamide mg/m^2) 100 followed by weekly paclitaxel as NAC, between December 2005 and February 2010, we have experienced 5 cases (5.3%) that had to discontinue NAC because of IP. We, herein, report the clinical course of these 5 patients, and discussed the importance of early diagnosis and treatment for immediate recovery from IP during NAC, in order not to make critical delay in following plan of scheduled anti-cancer therapy.

Results: In all cases, we could start the therapy for IP within 2 weeks from the appearance of initial symptoms. IP was completely healed only by the interruption of the chemotherapeutic agent in a case. While, steroid pulse therapy was effective in 2 cases, and prolonged administrations of prednisolone for 3 weeks were necessary in other 2 cases. Admission was required in 3 cases because of the hypoxia. In all cases, curative operation was accomplished 3 to 6 weeks after last administration of anti-cancer drug.

Conclusion: In order not to postpone the operation, it is important to diagnose interstitial pneumonia during NAC by chest CT and treated by steroid pulse therapy without delay.

PO04-16

SKIN SPARING MASTECTOMY AND IMMEDIATE BREAST RECONSTRUCTION: THE VALUE OF LATISSIMUS DORSI MUSCULOCUTANEOUS FLAP

Zisun Kim[1], Sang-gue Kang[2], Min Hye An[1], Jihyoun Lee[1], Hyuk Mun Kim[3], Sun Wook Han[3], Sung Yong Kim[3], Chul Wan Lim[3], Min Hyuk Lee[1]

[1]*Department of Surgery, Soonchunhyang Univ. Seoul Hospital, Korea*
[2]*Department of Plastic and Reconstructive Surgery, Soonchunhyang Univ. Seoul Hospital, Korea*
[3]*Department of Surgery, Soonchunhyang Univ. Bucheon Hospital, Korea*

Background/Purpose: Skin sparing mastectomy (SSM) and immediate breast reconstruction (IBR) is a tailored surgical procedure in operable breast cancer. The surgical outcome of our SSM and latissimus dorsi (LD) flap IBR was assessed.

Methods: Between March 2000 and February 2011, 145 consecutive patients underwent SSM and IBR. Among 85 patients (58.6%) who were eligible for questionnaire survey, 65 patients who underwent SSM and LD flap IBR without a prosthetic implant were included in the study. A stratified analysis was performed to assess the surgical outcome, as well as the degree of patient satisfaction.

Results: The mean age of the patients was 48.4 years (range, 21-74), and the pathologic results were infiltrating ductal carcinoma in 48 patients (73.8%), ductal carcinoma *in situ* in 15 (23.1%), and others in 2 (3.1%). After a mean follow-up period of 34 months (range, 1.6-89.9) no local recurrence occurred, and 1 patient (1.5%) developed an axillary metastasis. There were no cases of LD flap necrosis or flap loss. Donor site morbidities occurred in 22 patients; seroma in 8 (12.3%), scarring in 8 (12.3%), and back pain in 6 (9.2%). Fifty patients (76.9%) were satisfied and 40% reported their degree of satisfaction as excellent. Breast symmetry ($p < 0.001$), nipple cosmesis ($p < 0.001$), panel assessment ($p < 0.001$), and visual difference of bilateral breasts ($p = 0.021$) were factors that affected the higher patient satisfaction.

Conclusion: Our SSM and LD flap IBR was safe with low morbidities, and sufficiently produced a high level of patient satisfaction. Achieving breast symmetry and nipple cosmesis would be the key to meet the patient's expectations.

Poster Discussion

PO04-17

SHORT-TERM OUTCOMES OF IMMEDIATE BREAST RECONSTRUCTION USING IMPLANT OR TISSUE EXPANDER AFTER MASTECTOMY IN BREAST CANCER PATIENTS

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Background/Purpose: Mastectomy is a life-saving management but can cause significant adverse reactions. So, breast reconstruction is a concern in recovery after mastectomy. We report our experience with immediate breast reconstruction using implant or tissue expander, which confirmed the oncologic safety and high patients' satisfaction.

Methods: This study is a retrospective review of all patients who underwent reconstruction with implant or tissue expander immediately after mastectomy. Seventy-three patients underwent breast reconstruction at Cheil general hospital breast cancer center from July of 2007 to November of 2010 and 14 patients were excluded because of follow-up loss. Therefore 59 patients were included. To access patient's satisfaction, questionnaire was sent to all patients.

Results: After median follow-up periods of 22.2 months, there was 1 case of locoregional recurrence and overall breast cancer specific survival was 100%. Overall major complication rate was 18.6% (11 patients), such as nipple areolar complex (NAC) necrosis and implant removal. Among 7 patients who had NAC necrosis, 2 patients improved after observation, and 5 patients had NAC excision. Four patients were removed their implant due to severe infection. According to the result of questionnaire, 77.6% was satisfied with generalized operational result, 71.4% with cosmetic result. There were 12 cases of skin sparing mastectomy (SSM), 22 cases of NAC preserving mastectomy, and 10 cases of NAC preserving SSM. Among these 22 patients, 79.2% was satisfied with general result, 75% with cosmetic result.

Conclusion: Immediate breast reconstruction after mastectomy is oncologically safe procedure as well as relatively good patient's satisfaction. But we need more long-term experience.

PO04-18

CHEST WALL RECONSTRUCTION WITH THORACOABDOMINAL FLAP AND THORACOEPIGASTRIC FLAP FOR LARGE SKIN DEFECTS AFTER MASTECTOMY OF ADVANCED BREAST CANCER

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[1]Department of Surgery, Graduated School of Medicine, Kyungpook National Univ., Korea
[2]Department of Plastic and Reconstructive Surgery, Graduated School of Medicine, Kyungpook National Univ., Korea

Background/Purpose: Radical surgical extirpation in advanced breast cancer patients produces extensive loss of skin with large defects requiring plastic surgical procedures for the closure. Many reconstructive methods exist, the choice of which depends upon the characteristic of the wound, extent of resection and patient comorbidities.

Methods: For adequate coverage of the large skin defects following resection of advanced breast cancer, current authors have performed a thoracoabdominal flap and a thoracoepigastric flap.

Results: In thoracoabdominal flap (Fig. 1), flap dissection is entirely performed in a prefascial plane and the flap involving external oblique abdominal muscle. The flap is rotated clockwise in left chest wall defects and counterclockwise in right chest defects and the donor site was closed directly. The thoracoepigastric flap (Fig. 2) is based on perforators originating from the intercostals vessels through the rectus abdominis or the external oblique muscles. Due to an abundant presence of skin and subcutaneous tissue under the breast, the primary suture can mostly be performed for the donor site of a flap. The raised flap is transpositioned in advance and the flap is sutured on the defect.

Conclusion: Large chest wall reconstructions are usually required after radical excision of advanced cancer stages patients with poor general conditions. Thoracoabdominal flap and thoracoepigastric flap are simple, quick single-stage procedures, and offer to patient fast recovery, low complication rate, enabling further concomitant adjuvant therapy.

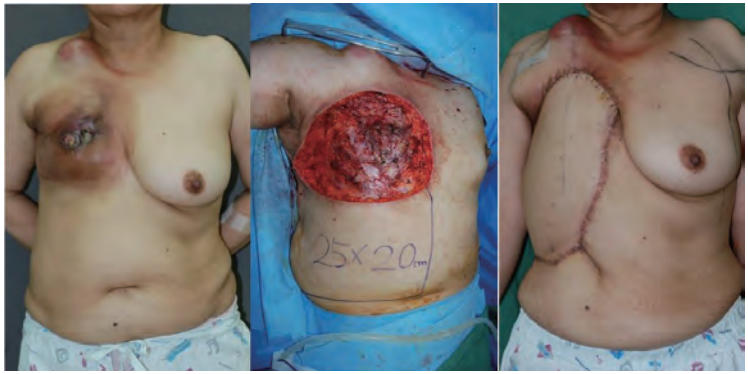

Fig. 1

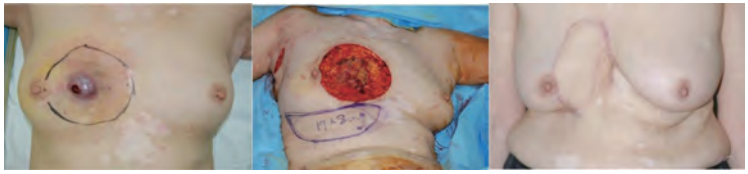

Fig. 2

PO04-19

THE PROGNOSTIC VALUE OF THE NODAL RATIO IN N1 BREAST CANCERS

Tae Jin Han[1], Eun Young Kang[2], Sung Won Kim[2], Jee Hyun Kim[2], So Yeon Park[2], Jae Sung Kim[1], In Ah Kim[1]

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[2]*Breast Care Center, Seoul National Univ. Bundang Hospital, Korea*

Background/Purpose: Adjuvant regional radiation therapy is a highly controversial treatment for breast cancer patients with one to three positive nodes (N1). We evaluated the predictive value of the nodal ratio (NR) and identified other clinicopathologic variables associated with poor prognosis in these patients.

Methods: We analyzed 130 patients with N1 invasive breast cancer. Disease-free survival (DFS), locoregional recurrence-free survival (LRRFS), and distant metastasis-free survival (DMFS) were compared according to the NR with a cut-off value of 0.15.

Results: The NR was statistically independent from other prognostic variables in the chi square test. On univariate analysis, patients with a NR >0.15 had significantly lower 5-year LRRFS and 5-year DMFS and marginally lower 5-year DFS than those with a NR ≤ 0.15, respectively. On multivariate analysis, a NR >0.15 significantly correlated with lower DFS and DMFS, but not LRRFS. Since the predictive power of the NR on LRRFS and DMFS was found to differ with diverse clinical and pathologic variables, we performed adjusted analysis stratified by age, pathologic characteristics, and adjuvant treatments. Only young patients with a NR >0.15 showed significantly lower DFS as well as those presenting an unfavorable pathologic profile such as advanced T stage, histologic grade 3, positive lymphovascular invasion, involved resection margin, and no adjuvant treatment.

Conclusion: A NR >0.15 was associated with an increased risk of locoregional recurrence and distant metastasis, especially in young patients with unfavorable pathologic profiles. Therefore, NR may be a useful indicator to be considered when deciding whether to use adjuvant nodal radiotherapy to treat patients with N1 disease.

Poster Discussion

PO04-20

PARTIAL BREAST RECONSTRUCTION USING ONCOPLASTIC TECHNIQUES IN CENTRALLY LOCATED BREAST CANCER

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Background/Purpose: The use of breast-conserving surgery has significantly increased in recent years. However, centrally located breast cancer is difficult to manage using breast-conserving treatment. This study describes the use of oncoplastic techniques for centrally located breast cancer in immediate partial mastectomy reconstruction.

Methods: From January of 2007 to January of 2010, various kinds of oncoplastic techniques were used in 25 patients with centrally located breast cancer. The different method of oncoplastic techniques were chosen according to the ratio of breast volume to resection volume (Fig. 1, 2).

Results: The mean age was 51 and the average follow up interval was 11 months. If the breast size is small to moderate and defect is smaller than 100 g, purse string suture (n = 6), linear suture (n = 7) and regional flap such as thoracoepigastric flap (n = 2), adipofascial flap (n = 1) were selected. And the defect exceed 100 g, LD flap (n = 3) and thoracodorsal artery perforator flap (n = 3) was done. In case of the breast size is large and defect is larger than 150 g, reduction mammoplasty was usually performed (n = 3). There were two partial skin necrosis during the follow up periods, which was spontaneously resolved. In this study, most of the patients of the patients were satisfied on the cosmetic outcome.

Conclusion: Partial breast reconstruction using oncoplastic techniques in centrally located breast cancer could be a reasonable and safe option for breast cancer patients who desire conserving surgery with aesthetical breast.

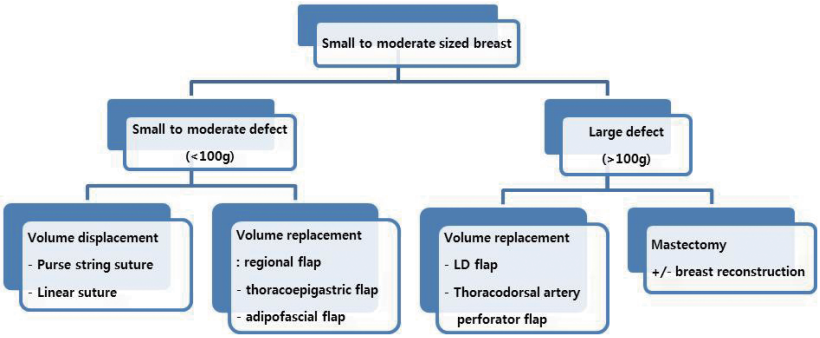
Small to moderate sized breast
Small to moderate defect
(<100g)
Large defect
(>100g)
Volume displacement
- Purse string suture
- Linear suture
Volume replacement
: regional flap
- thoracoepigastric flap
- adipofascial flap
Volume replacement
- LD flap
- Thoracodorsal artery
perforator flap
Mastectomy
+/- breast reconstruction

Fig. 1

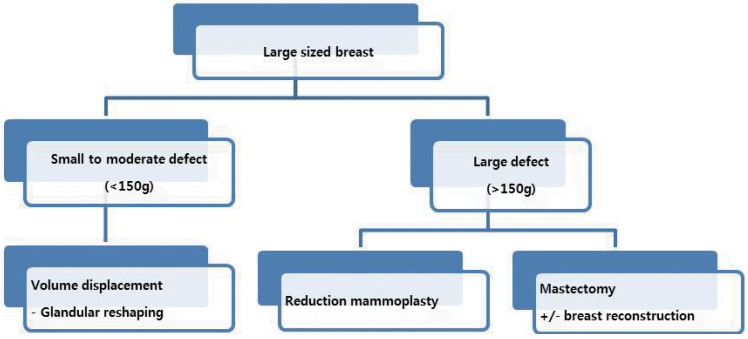
Large sized breast
Small to moderate defect
(<150g)
Large defect
(>150g)
Volume displacement
- Glandular reshaping
Reduction mammoplasty
Mastectomy
+/- breast reconstruction

Fig. 2

PO04-21

LUMPECTOMY WITH OR WITHOUT RADIATION THERAPY FOR THE TREATMENT IN DUCTAL CARCINOMA *IN SITU* OF BREAST: SINGLE INSTITUTE EXPERIENCE

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Background/Purpose: To compare local recurrences between lumpectomy and lumpectomy with radiation therapy in ductal carcinoma *in situ* (DCIS) of breast.

Methods: From December 1999 to September 2006, 40 patients with DCIS were treated with lumpectomy with or without radiation therapy of breast DCIS at Keimyung University Dongsan Medical Center. Fifteen patients were treated with lumpectomy and twenty five treated with lumpectomy followed by radiation therapy (radiotherapy group). The range of age was from 28 to 64 (median 44). Total dose 45-50.4 Gy (median 50.4) was irradiated through 5 days a week, 1.8 Gy once a day using tangential fields with/without boost radiation 10-16 Gy to tumor bed. The range of follow-up periods was from 55 to 139 months (median 85).

Results: There were statistically significant differences of patient distribution in grade, comedo type and tumor size between lumpectomy and radiotherapy group, but not in age, necrosis and margin status. There were more patients with high grade tumors and large sized tumors in radiotherapy group. There was no difference in local recurrence. Ipsilateral breast recurrences were observed in two patients, one patient in lumpectomy group and the other in radiotherapy group. They also had hormonal therapy with tamoxifen after lumpectomy. Contralateral invasive breast cancer developed in one patient with radiation therapy.

Conclusion: Although radiation therapy was performed in more unfavorable patients, there was no difference in local recurrence. Therefore, we thought radiation therapy might improve local control rate in both favorable and unfavorable patients. Further larger studies need to be performed to evaluate effectiveness of radiation therapy in DCIS of breast.

PO04-22

PARTIAL BREAST RECONSTRUCTION USING REDUCTION MAMMOPLASTY TECHNIQUES IN BREAST CANCER PATIENTS

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Background/Purpose: Breast-conserving surgery (BCS) for breast cancer has been a widely used treatment protocol. Among oncoplastic technical options, the reduction mammoplasty remains a useful procedure in patients with large or ptotic breasts. The purpose of this study was to analyze the feasibility of the technique and its outcome following conservative breast surgery.

Methods: From September of 2007 to May of 2011, 22 patients were performed for breast reconstruction. These techniques were indicated to reconstruct defects more than moderate size in patients with moderate or large breast. The patients were divided into three groups: superior pedicle group, inferior pedicle group, glandular reshaping group. Depending on the incision type, inverted T incision or vertical incision was carried out in each group.

Results: The mean age was 48.9 years and the average follow up interval was 11 months. 22 patients underwent immediate reduction mammoplasty with superior pedicle (n = 9), inferior pedicle (n = 5) and glandular reshaping (n = 8) following BCS (Table 1). Inverted T incision was made in 13 patients and vertical incision in 9 patients. Contralateral breast surgery was usually required to restore the symmetry. The average specimen weight was 305 g. The majority of patients were satisfied at the cosmetic result that evaluated in 10 months. Breast complication was developed in 3 cases including 2 wound dehiscences, 1 wound infection and 1 fat necrosis.

Conclusion: Therapeutic mammoplasty is a useful procedure for shape and symmetry preservation in women with large or ptotic breasts by creating symmetric, aesthetically pleasing breasts (Fig. 1).

Mean age, year			48.86±10.4
Mastectomy Extent	Surgical Technique	Incision Type	n (%)
Nipple Saved	Superiorly Based Dermal Pedicle	Wise Pattern (Inverted T)	5 (22.7)
		Vertical Pattern	4 (18.2)
	Inferiorly Based Dermal Pedicle	Wise Pattern (Inverted T)	4 (18.2)
		Vertical Pattern	1 (4.5)
Nipple Abandoned	Glandular Reshaping	Wise Pattern (Inverted T)	4 (18.2)
		Vertical Pattern	4 (18.2)
Total Cases			22 (100%)

Table 1.

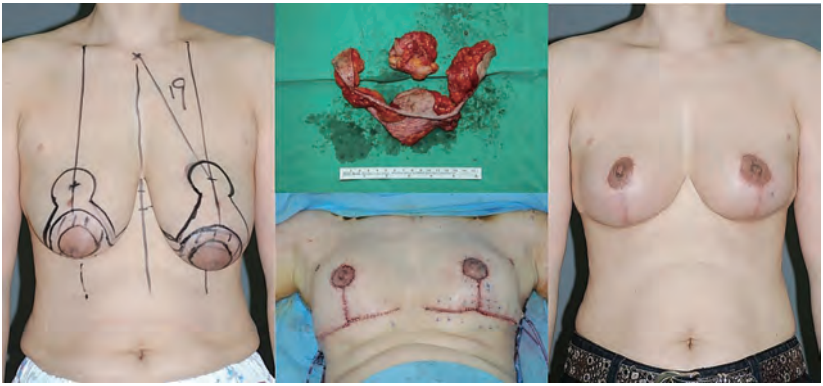

Fig. 1

PO04-23

CLINICAL OUTCOME OF CENTRAL NERVOUS SYSTEM METASTASES FROM BREAST CANCER: DIFFERENCES IN SURVIVAL DEPENDING ON SYSTEMIC TREATMENT

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Background/Purpose: Central nerve system (CNS) metastases are a feared complication of breast cancer and are associated with poor prognosis. The purpose of this study is to investigate the clinical characteristics of CNS metastases and to clarify the prognostic factors after CNS metastases in breast cancer at a single institution over a long time period.

Methods: We retrospectively reviewed the medical records of breast cancer patients diagnosed at Seoul National University Hospital from 1981 to 2009 and identified the patients who experienced CNS metastases. We collected the data including demographics, clinico-pathologic characteristics, dates of diagnosis of original breast cancer and subsequent metastases, date of death and correlated the findings with the clinical outcome.

Results: Total of 400 patients were identified, 17 patients (4.3%) were diagnosed CNS metastases with primary breast cancer concurrently and 383 (95.7%) experienced CNS metastases subsequently after the diagnosis of primary breast cancer. The patients with good performance status (PS), initial CNS metastasis as recurrence, absence of extracranial metastases, non-visceral extracranial metastases, longer interval from the date of primary breast cancer to the date of CNS metastasis, chemotherapy (CTx) after whole

Poster Discussion

brain radiotherapy (WBRT) and gamma-knife surgery (GKS) had better outcomes in univariate analyses. In multivariate analysis, good PS, systemic CTx after WBRT, GKS, and longer interval to CNS metastasis, were independent prognostic factors for overall survival after CNS metastases.

Conclusion: Our results suggest that appropriate palliative systemic therapy after WB-RT or GKS, adequate palliative treatment via combined modalities are helpful for breast cancer patients, even after the detection of CNS metastases.

PO04-24

THE PROPER TECHNIQUES FOR IMMEDIATE RECONSTRUCTION AFTER MASTECTOMY IN KOREAN WOMAN WITH SMALL OR MEDIUM SIZED BREAST

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Background/Purpose: The patient's desire for reconstruction surgery as well as radical surgery has become to increase in breast cancer. However, it is generally difficult to obtain both of curable and cosmetic purpose in mastectomy. Oncoplastic surgery in breast cancer is considered to get both of curability and good cosmetic result. We analyzed cosmetic results and complications of various reconstruction techniques to find adequate reconstruction methods for Korean woman with small or medium sized breast.

Methods: From July 2008 to June 2011, we tried to manage deformity after mastectomy by using various methods such as oncoplastic surgery, augmentation, and mesh insertion. We tried to apply oncoplastic mammoplasty in 65 patient and augmentation after skin sparing mastectomy in 43 patients. Thirty-five patients were inserted absorbable Vicryl Mesh® into the defect after partial mastectomy.

Results: The cosmetic outcomes for the oncoplastic mammoplasty were excellent or good in 55 cases (84.6%) and fair in 10 cases. Ten cases (23.4%) showed good cosmesis in augmentation after skin sparing mastectomy. The cosmetic results for absorbable mesh insertion technique were good in 15 (42.9%), but poor in 20 (57.1%). Absorbable mesh insertion has showed many adverse effects such as erythema, seroma, contracture, and chronic pain. Significant portion of cases were needed reoperation because of severe complication.

Conclusion: Immediate reconstruction using oncoplastic surgery showed good cosmetic results and high satisfaction for most Korean woman with small or medium sized breasts. But the absorbable mesh insertion doesn't seem to be a safe method to prevent deformity after partial mastectomy.

PO04-25

OUTCOMES IN POSTMENOPAUSAL WOMEN OF T2N0 BREAST CANCERS WITHOUT ADJUVANT CHEMOTHERAPY

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Background/Purpose: Systemic therapy for breast cancer patients after surgery is important. It reduces the recurrence rate and mortality rates. Chemotherapy is currently one of the most types of breast cancer treatments. However, chemotherapy is not effective for everyone and has certain side effects. Whether the expression of hormone receptors influences the degree of benefit from chemotherapy has been debated for many years. chemotherapy in older women diagnosis with low-risk, hormone receptor-positive breast cancer still inspires controversy.

Methods: Between May 2003 and July 2008, 5.695 patients had operation on invasive breast cancer in Asan Medical Center. One hundred forty two cases of pT2N0 breast cancers with median follow-up of 61 months were reviewed. 103 patients were treated with chemotherapy followed by endocrine therapy. 39 patients were treated with endocrine therapy alone.

Results: A patient age < 60 ($p = 0.001$), a high histologic grade ($p = 0.020$) and C-erbB2 overexpression ($p = 0.003$) were more frequent for the chemotherapy group. However, there were no statistically significant differences in disease-free and overall survival between the treatment group.

Conclusion: We believe that some postmenopausal women with T2N0 breast cancer can avoid chemotherapy.

PO04-26

LAPATINIB WAS HIGHLY EFFECTIVE IN THE TREATMENT OF A CASE OF MULTIPLE LIVER METASTASES OF BREAST CANCER AFTER SURGERY

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Background/Purpose: Lapatinib is a molecular targeted drug for patients with a recurrence or progression breast cancer after chemotherapy with anthracycline drugs, taxanes or trastuzumab. Here we report a case of a marked reduction in multiple liver metastases of postoperative breast cancer treated by lapatinib.

Methods: The patient was a 54-year-old woman who underwent a right mastectomy for breast cancer in 2005. The pathological results revealed papillotubular carcinoma, N1 (2 metastatic nodes out of 23 lymph nodes), ER (-), PgR (-), HER2 (3 +). Moreover, she underwent 3 cycles of adjuvant chemotherapy with Fluorouracil Epirubicin Cyclophosphamide (FEC).

Results: In 2007, she was found to have bone metastases, multiple brain metastases and multiple liver metastases, despite treatment with capecitabine, TS-1, paclitaxel, trastuzumab, and vinorelbine. In 2008, she presented with bile duct stenosis presented due to an increase in liver metastases, and was admitted for the placement of a biliary stent. Thereafter, she received lapatinib treatment as an outpatient, and liver metastases were reduced.

Conclusion: The liver metastases have been controlled for two years. Here we report on related literature and discuss the highly effective treatment of cases by lapatinib.

PO04-27

MAMMOTOME EXCISION FOR BENIGN BREAST DISEASE - 6264 CASES EXPERIENCE IN A SINGLE INSTITUTE

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Background/Purpose: In recent years, with the advancement of Mammotome (MMT) instruments and procedural techniques, there have been many trials to remove the benign lesions with curative intension. The aim of this study was to evaluate the efficacy and the safety of the MMT biopsy device for percutaneous removal of breast masses with ultrasonic guidance (USG).

Methods: From January 2003 to April 2011, a total of 6,264 USG excisional MMT biopsies were performed in 4,942 patients at Kangnam Cha Hospital. Those lesions with BI-RADS category 3, 4Ac and 5 by ultrasonic examination were included in this study. Lesions below 1.0 cm were removed by an 11 gauge probe, and lesions above 1.0 cm were removed by an 8 gauge probe. Ultrasonographic follow-ups were performed 3 to 6 months later to assess the residual tissue and scarring.

Results: The mean patient age was 37.0 (range: 13-95) years. The average size of lesion was 1.22 cm (SD = 0.74 cm). Among the patients, 60.6% had non-palpable lesion and 39.4% had palpable tumor. The majority of the specimens (96.1%) were benign. 52.2% (3,274 lesions) had fibroadenoma, 20.7% (1,295 lesions) had fibrocystic changes, 3.3% (208 lesions) had intraductal papilloma and although 244 lesions (3.9%) were malignant. The mean MMT procedure time was 3.7 ± 2.7 minutes and the mean number of cores removed was 10.4 ± 9.3.

Conclusion: Percutaneous breast biopsy with the MMT system may be feasible and effective for the diagnostic and therapeutic management of benign breast lesions. Instead of the open biopsy, it may be safely performed for the lesions less than 3 cm.

Figure 1. Patient age and tumor size distribution.

Age (Years)	Numbers of patients (%)	Graph
10~19	41 (0.8)	
20~29	1081 (21.9)	
30~39	1956 (39.6)	
40~49	1332 (26.5)	
50~59	437 (8.6)	
Above 60	95 (1.9)	
Total	4942 (100.0)	0 1000 2000 3000

Size(cm)	Numbers of lesions (%)	Graph
≤ 0.5	627 (10.0)	
0.6~1.0	2542 (40.6)	
1.1~1.5	1691 (27.0)	
1.6~2.0	732 (11.7)	
2.1~3.0	476 (7.6)	
> 3.0	196 (3.1)	
Total	6264 (100.0)	0 500 1000 1500 2000 2500

Fig. 1

Table 1 Patient(n=4942) and Pathologic(n=6264) characteristics.

Palpable lesions	2470 cases (39.4%)
Non-palpable lesions	3794 cases (60.6%)
Right	2103 patients (42.6%)
Left	2216 patients (44.8%)
Bilateral	623 patients (12.6%)
USG BI-RADS category 3	4044 cases (64.6%)
category 4a-c, 5	2220 cases (35.4%)
Breast cancer diagnosed	244 cases (3.9%)
	23/4044 (0.57%) in category 3 221/2220 (9.9%) in category 4a-c, 5

Pathology	Numbers of lesions(%)
Fibroadenoma	2965 (47.3)
Fibroadenoma c ductal epithelial hyperplasia	308 (4.9)
Fibrocystic disease	1295 (20.7)
Sclerosing adenosis	77 (1.2)
Intraductal papilloma	208 (3.3)
Ductal epithelial hyperplasia	124 (2.0)
Malignancy	244 (3.9)
Phyllodes tumor	48 (0.8)
Atypical ductal epithelial hyperplasia	10 (0.2)
Other benign diseases	985 (15.7)
Total	6264 (100)

Table 1.

PO04-28

PERCUTANEOUS RADIOFREQUENCY ABLATION OF BREAST CANCER LIVER METASTASES

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Background/Purpose: While systemic chemotherapy remains the mainstay of treatment for metastatic breast cancer, ultrasonography (US)-guided percutaneous Radiofrequency ablation (RFA) has been utilized to control liver metastasis.

Methods: We retrospectively assessed patients who underwent US-guided RFA between January 2002 and April 2011 for a long term efficacy.

Results: A total of 10 patients underwent RFA (one lesion/patient). Although all patients achieved complete tumor dormancy, 3 patients developed recurrence at the RFA site and 7 developed new liver lesions with a median follow-up of 11.8 months. Overall survival was 18.6 months with 1-year survival rate of 68%.

Conclusion: US-guided RFA is a therapeutic option for selected patients with liver metastasis.

case	Age at RFA, yr	DFI, yr	ER/PR/HER2 (1°tumor) liver biopsy	1° mets to liver mets, yr	Liver mets to RFA, mo	Size of liver mets	Other mets site at RFA	Liver _TTP, mo	OS from RFA, mo	Cause of death
1	57	5.3	+/+/-	0	3.4	2.0		15.6	28.1	Liver
2	47	4.9	-/-/-	9.0	0.3	3.0		1.1	19.6	Lung
3	51	1.8	-/-/+	0	1.1	2.7		2.8	10.3	Liver
4	51	5.0	(-/-/-)	2.7	4.5	3.1	Lung	19.2	24.5	Peritoneal
5	54	2.2	(-/-/+)	0	20.9	2.0		4.7	10.5	Liver
6	46	1.5	+/+/-	0	0.5	3.3	Lung	1.7	4.1	Lung
7	44	4.0	(+/+/-)	0	23.8	2.4	Lung	9.0	31.9	Unknown
8	36	0.3	+/-/+	0	1.6	1.6	Bone, LN	40.7+	40.7+	Alive
9	57	6.7	-/+/-	0	0.5	2.4		3.2	13.4	Liver
10	33	4.0	+/+/-	0	4.5	2.3		0.5+	0.5+	Alive

Table 1. Case summary of breast cancer liver metastases underwent US-guided RFA

Abbreviation: DFI = disease free interval, yr = year, 1°tumor = primary tumor, mets = metastases

Table 1.

PO04-29

DOES IMMEDIATE BREAST RECONSTRUCTION AND THE TYPE OF RECONSTRUCTION INFLUENCE THE INITIATION OF ADJUVANT CHEMOTHERAPY?

Jeonghui Lee, Se Kyung Lee, Sangmin Kim, Min Young Koo, Min-young Choi, Soo Youn Bae, Dong Hui Cho, Jiyoung Kim, Seung Pil Jung, Jun-ho Choe, Jung-han Kim, Jee Soo Kim, Jeong Eon Lee, Jung-hyun Yang, Seok Jin Nam

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Background/Purpose: The frequency of immediate breast reconstruction (IBR) is increasing, and the types of reconstruction used are diverse. Our aim was to determine how IBR and type of reconstruction affect the time to initiation of chemotherapy.

Methods: We retrospectively analyzed the electronic patient database and medical treatment records from 2008 to 2010 at our hospital.

Results: We compared 43 patients who underwent IBR (study group) to 552 patients who did not undergo IBR (control group) and found a significant difference in time to initiation of chemotherapy ($p < 0.0001$). There were no cases of delays of more than 12 weeks. There were no significant differences in the time to chemotherapy according to the type of reconstruction ($p = 0.095$).

Conclusion: IBR delays the initiation of chemotherapy, but does not lead to omission or significant clinical delay in chemotherapy. Further, the type of reconstruction does not affect the time to chemotherapy.

PO04-30

USE OF POLIGLECAPRONE SUTURE ENCAPSULATED ABSORBABLE ADHESION BARRIER FOR FOCAL DEFECT OF BREAST

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Background/Purpose: Numerous oncoplastic techniques with absorbable materials had been reported for breast conserving surgery. Authors report the clinical application of poliglecaprone suture with absorbable adhesion barrier instead of expensive polyglycolic acid mesh to filling focal defect of breast according to oncoplastic techniques.

Methods: Between January 2009 and March 2011, 25 female patients with breast cancer undergone oncoplastic surgery with poliglecaprone suture(Monocryl®) encapsulated absorbable adhesion barrier(Interceed®). After interceed pocket which was sewn with poliglecaprone suture was turned inside out, ten to fifteen pieces of 5 cm- poliglecaprone suture were put into the pocket. Then the compound was inserted to focal defect of breast and double skin technique was performed. The cosmetic outcomes were estimated by four-point scoring system by patient herself.

Results: Mean age of patients was 51.8 years (range, 27-75). After tumor resection with 2 cm of safety margin, nine patients were performed rotational local flap and two patients were latissimus dorsi myocutaneous flap with poliglecaprone suture encapsulated absorbable adhesion barrier. Mean volume loss of breast was 84.3 g (range, 28.1-270.1) and mean tumor size was 2.3 cm (range, 1.0-9.0). Tumor types were invasive ductal carcinoma in 20 cases and ductal carcinoma *in situ* in 5 cases. Although the drainage tube was not inserted, there was no significant complication such as seroma or infection. The cosmetic outcome was excellent in 8 cases, good in 11 cases and fain in 6 cases.

Conclusion: Using of poliglecaprone suture encapsulated absorbable adhesion barrier would be useful volume replacement technique for focal deformity without significant complication after breast conserving surgery.

Fig. 1

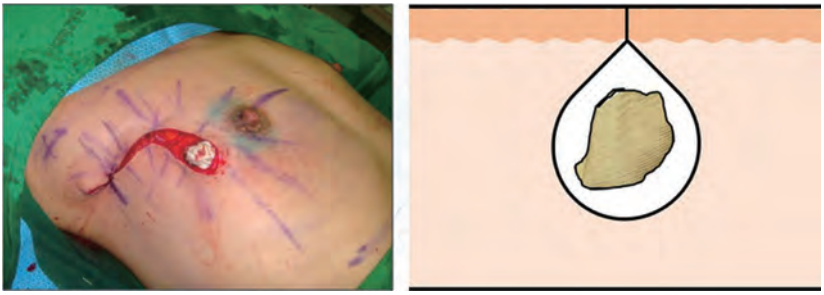

Fig. 2

PO04-31

COMBINATION OF TWO LOCAL FLAPS FOR LARGE DEFECTS OF THE BREAST

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Background/Purpose: Oncoplastic surgery (OPS) has emerged as a new technique for wide excision of breast cancer without compromising the natural shape of breast. But, there are some difficulties to perform simple local flap when the cancer is located in upper inner or medial portion. Authors have combined two local flaps, referred to as a 'combined local flap' for large defects of the breast after a partial mastectomy.

Methods: Twenty-one patients with breast cancer underwent a partial mastectomy with a combined local flap. Combined pedicle flap is defined as rotational local flap and a thoracoepigastric flap (TEF). The most important vascular feeding of TEF is from the fascia of underlying muscles. And the breast cosmetics were estimated by four-point scoring system of breast cosmesis.

Results: Twenty-one patients were treated with the combined pedicle flap after breast conserving surgery. The mean age of patients was 53.3 years and the mean tumor size was 2.2 cm. The mean excised breast volume was 133.8 mm^3 and the percentage of excised volume was 20.4%. The cosmetic outcomes were judged as excellent, good, and fair in 11, 8, and 2 cases, respectively.

Conclusion: Although the two of breast scar remains, breast shape could be maintained with combined pedicle flap. The combined local flap, consisting of a rotational local flap and a TEF is a useful oncoplastic technique for large defects of the breast.

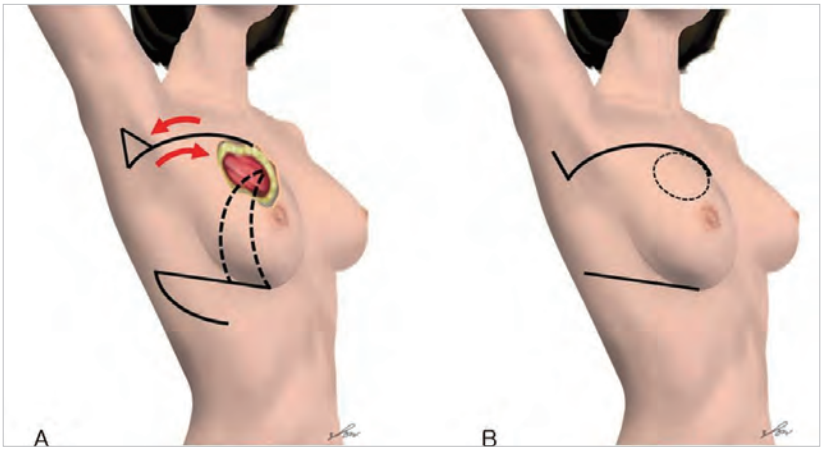

Fig. 1

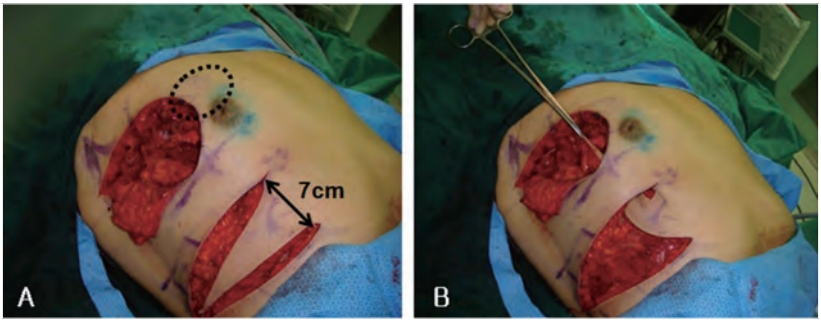

Fig. 2

PO04-32

RELIABILITY OF COMBINED SENTINEL LYMPH NODE BIOPSY AND DYE-ASSISTED COMPLEMENTARY NODE SAMPLING TECHNIQUE IN INTRAOPERATIVE AXILLARY STAGING FOR BREAST CANCER IN A DISTRICT HOSPITAL

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Background/Purpose: Current literature suggests that the radiolabelled colloid, lymphoscintigraphy and blue dye offer the fewest false negative rate in axillary staging. However, in a district hospital where radioisotope facilities are not feasible, we postulated that a combination technique of sentinel lymph node (SLN) biopsy with dye-assisted complementary node (CN) sampling intraoperatively yields equivalent success rate.

Methods: Over 14 months, 112 patients with clinically and radiologically node-negative breast cancer underwent SLN biopsy during mastectomy or wide local excision. Patent blue dye was injected peritumourally before surgery. Blue stained SLNs and suspicious complementary nodes were identified visually and from palpation. Patients with positive frozen section (FS) diagnosis proceeded to axillary clearance.

Results: The median numbers of blue-stained SLNs and complementary nodes excised were 2 and 3, respectively. FS (false negative rate = 18%, sensitivity 82%, accuracy 96.4%) alone correctly predicted nodal metastasis in 16% of cases, 19.6% with paraffin section (PS). Sensitivity and false negative rate for combination of FS and PS was 92.2% and 7.8%. Another further 7 cases of metastasis were identified from CN when both FS and PS were negative, giving a detection rate of 100%. SLNB alone would have understaged 6.3% of axillae.

Conclusion: We recommend that surgeons should sample at least 3 CNs along with the blue-stained SLNs to safely and reliably perform axillary staging intraoperatively when sophisticated facilities are not available.

PO04-33

NOVEL QUINUCLIDINONES DERIVATIVES INDUCES APOPTOSIS IN HUMAN MCF-7 BREAST CANCER CELLS VIA SPHINGOMYLINASE SIGNALING PATHWAY

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Background/Purpose: We previously reported novel quinuclidinone derivatives that cause cytotoxicity in human non-small lung carcinoma epithelial cells null for p53 (H1299). The current study investigates the effect of novel set of quinuclidinone derivatives on cytotoxicity of human MCF-7 cells and normal breast epithelial cells (MCF-12a).

Methods: The effects of the analogs were investigated by MTT assay, clonogenic survival assay, sphingomylinase activity, ELISA based apoptotic assay, TUNEL assay, immunofluoresence staining, flow cytometry, real time RT-PCR and Western blot analysis.

Results: This study shows that quinuclidinone derivatives 4 and 6 induce growth inhibition mainly through apoptosis of breast cancer cells (MCF-7) with less cytotoxic effect in normal breast epithelial cells (MCF-12a) for derivative 6 while derivative 4 induced similar cytotoxicity for both breast cancer cells and normal breast epithelial cells. Derivative 6 induced G1 phase arrest presumably to sensitize the breast cancer cells to apoptosis by increasing expression level of p21 and cyclin E. Moreover, derivative 6 increased expression level of ERK1, p53 and Bax, and it reduced expression level of Akt and Bcl-2. By investigating the sphingomyelinase apoptosis pathway, it was observed that derivative 6 significantly increased sphingomylinase activity and increased formation of ceramide as well as increased expression levels of JNK-phoshortlation, caspase 8 and caspase 9 and Parp-1 cleavage.

Conclusion: Based on previous results it is proposed that quinuclidinone derivative 6 provokes apoptosis in human breast cancer cells (MCF-7) via the sphingomylinase pathway.

PO04-34

RELATIONSHIP BETWEEN HISTOPATHOLOGICAL EVALUATION OF NEOADJUVANT CHEMOTHERAPY AND MRI VOLUMETRY REDUCTION RATES

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Background/Purpose: We use ultrasound and MRI to evaluate the effectiveness of neoadjuvant chemotherapy in breast cnacer patients. The aim of this research was to investigate the relationship between Histopathological evaluation of neoadjuvant chemotherapy for primary breast cancer and MRI volumetry reduction rates, and to analyze of comparision between RECIST and MRI volumetry.

Methods: We examine 42 patients (44 tumors) receiving neoadjuvant chemotherapy for primary breast cancer between October 2007 and September 2008. The median age was 51 years, range 33-70. MRI and ultrasound was used to examine breast tumors prior to after neoadjuvant chemotherapy. We used the Response Evaluation Criteria in Solid Tumors (RECIST) and MRI volumetry reduction rate to evaluate the efficacy of the treatments. And then, we examine the relationship between the result of RECIST or MRI volumetry reduction rate and histopathological criteria.

Results: Both RECIST and MRI volumetry correlate with Histopathological evaluation $p < 0.0001$. In 13 tumors, the pathological response were Grade3 (pCR), 6 tumors (46.2%) revealed cCR of RECIST, while 10 tumors (77%) revealed cCR of MRI volumetry. And then, MRI volumetry were useful to evaluate the efficacy of treatments for the non-mass region.

Conclusion: Compare with RECIST, MRI volumetry and histopathological evaluation of the effect of neoadjuvant chemotherapy of breast cancer were highly correlated. MRI volumetry was found to be useful to examine the effectiveness of neoadjuvant chemotherapy for primary breast cancer.

PO04-35

EFFICACY OF ZOLEDRONIC ACID FOR THE TREATMENT OF BONE METASTASES IN BREAST CANCER PATIENTS

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Background/Purpose: The purpose of this study was to evaluate retrospectively the efficacy of zoledronic acid for the breast cancer patients with bone metastases.

Methods: A total of 114 patients with bone metastases from breast cancer were assigned to treatment with 4mg zoledronic acid (n = 74) or no treatment (n = 40) between January 2003 and August 2010. Skeletal-related events (SREs) were defined as pathologic bone fracture, spinal cord compression, radiation therapy to bone, surgery to bone, and hypercalcemia of malignancy. Primary efficacy end points were the proportion of patients with at least one SRE and the time to first SRE.

Results: The percentage of patients with at least one SRE was reduced by 24% by zoledronic acid (19% vs. 43% for no treatment group). In addition, zoledronic acid consistently reduced the incidence of all types of SREs. The patients in the treatment group and those in the no treatment group had experienced one or more SREs in 21% and 35%, respectively. The patients with newly diagnosed bone metastases in the treatment group significantly delayed time-to-first SRE compared to the no treatment group.

Conclusion: Breast cancer patients with bone metastases who were treated with zoledronic acid had a low incidence of SREs compared to those without zoledronic acid. This study demonstrated the benefit of zoledronic acid for the prevention of skeletal complications.

PO04-36

THE RARE COMPLICATION CASES FOR EARLY BREAST CANCER AFTER BREAST-CONSERVING THERAPY

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Background/Purpose: In Japan, of all breast surgery about 60% has been included conserving surgery, and radiotherapy has been included about 80% in breast conservative surgery. We can usually find radiation dermatitis after radiotherapy. These are not serious. We report the rare complication after radiotherapy of early breast cancer in our institution.

Methods: The sample patients are 518 early breast cancer patients who underwent radiotherapy after breast-conserving surgery during April 1991 and May 2011. The radiotherapy procedure methods applied to the Japanese breast cancer society guideline, such as whole breast irradiation was performed 50 Gy per 25 fractions and boost irradiation was done 10 to 16 Gy per 5 to 8 fractions. The boost irradiation means an additional irradiation which indicates marginal positive or close margin positive cancer. We evaluate the rare complication cases which are induced or related radiotherapy.

Results: The rare complication cases were a movement of the clip set up in the tumor bed (The appearance rate within six months: 0.03%), rib deformities (The appearance rate within 6 months: 0.4%), and pneumonia during very-early stages for radiotherapy that is during radiotherapy and within 3 months after radiotherapy (The appearance rate: 0.04%)

Conclusion: There are no serious health problems for the rare complication after radiotherapy in early breast cancer patients. It is important for doctors to know and be aware of the above complications.

PO04-37

LACK OF ANY ASSOCIATION BETWEEN FUNCTIONALLY SIGNIFICANT CYP2D6 POLYMORPHISMS AND CLINICAL OUTCOMES IN EARLY BREAST CANCER PATIENTS RECEIVING ADJUVANT TAMOXIFEN TREATMENT

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Background/Purpose: Active metabolites of tamoxifen are formed mainly by the action of cytochrome P450 2D6 (CYP2D6). Since there are controversies regarding associations between CYP2D6 polymorphisms and outcomes among women with early breast cancer (EBC) treated with tamoxifen, the present evaluation of links with clinical outcomes was conducted.

Methods: We analyzed a total of 716 patients treated with tamoxifen for hormone receptor positive EBC between 2001 and 2005 at the National Cancer Center, Korea. All patients received tamoxifen 20mg/d for more than 6 months. DNA obtained from whole blood samples was genotyped for CYP2D6 variants associated with reduced (*10, *41) and absent (*5) activity.

Results: Of the total of 716 patients, 558 (77.9%) received adjuvant or neoadjuvant chemotherapy prior to the tamoxifen therapy. From the genotyping of CYP2D6, 152 (21.2%) patients were classified as having the wild type (W/W), 376 (52.7%) one variant allele (W/V), and 188 (26.1%) two variant alleles (V/V). Seventy (9.8%) patients experienced disease recurrence with a median follow-up of 5.6 (range, 0.6-10.3) years. Although known prognostic factors, including tumor size, nodal status, Ki67, progesterone receptor negativity, and HER2 positivity showed strong associations with the recurrence free survival (RFS) in this population, no significant association with any of the CYP2D6 genetic variants was evident ($p = 0.61$; hazard ratio [HR] = 1.14; 95% CI 0.68-1.92). This remained the case after subgroup analysis according to different adjuvant treatments.

Conclusion: Polymorphisms of CYP2D6 were not associated with clinical outcomes in EBC patients receiving adjuvant tamoxifen treatment.

PO04-38

OCCULT NIPPLE INVOLVEMENT IN BREAST CANCER

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Background/Purpose: The treatment of breast cancer has evolved, with treatment options including skin-sparing and nipple-sparing mastectomy. But few studies concerned the oncologic safety of preserved nipple-areolar complex. The purpose of this study is to evaluate the occult nipple involvement rate and improve patient selection for nipple sparing mastectomy.

Methods: We retrospectively analyzed 492 breast cancer patients with grossly unremarkable nipples who underwent mastectomy at the Department of Surgery, Kangbuk Samsung Hospital between 2005 and 2010. We reviewed patient clinical data and tumor pathologic report; age, tumor size, tumor-to-nipple distance, multifocality, multicentricity, lymph node metastasis, histologic grade, hormone receptor status, p53, HER2/*neu* status, lymphovascular invasion.

Results: Among patients underwent mastectomy, we found a 8.13% (40/492) rate of occult nipple positivity with histologic examination. Occult nipple involvement was statistically associated with tumor-to-nipple distance, multifocality, multicentricity ($p < 0.001$), and p53 status ($p = 0.036$).

Conclusion: More than 90% of breast cancer patients undergoing mastectomy did not have occult nipple involvement. This indicates that even patients who had clinically normal appearing nipple-areolar complex should be carefully selected for nipple sparing mastectomy.

PO04-39

PREDICTORS OF POSITIVE RESECTION MARGINS AFTER BREAST-CONSERVING SURGERY

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Background/Purpose: Positive resection margins are the most important factor associated with ipsilateral breast tumor recurrence after breast-conserving surgery (BCS). So, preoperative predictors of positive margins are required to avoid second operation.

Methods: A retrospective review of patients with invasive breast cancer and ductal carcinoma *in situ* (DCIS) between January 2003 and December 2005 was performed. Patients whose initial operation plan was BCS were included for assessing margin status.

Results: 794 patients met the inclusion criteria. In univariate analysis, microcalcifications on mammography (HR = 1.779, p = 0.002), breast density of grade 4 (HR 1.881, p = 0.003), DCIS component on pathology (HR = 2.447, p = 0.001), tumor size ≥ 2 cm on breast MRI (HR 1.788, p = 0.009), size discrepancy between breast MRI and ultrasonography > 0.5 cm (HR = 3.375, p < 0.0001), non-triple negative breast cancer (HR 3.853, p < 0.0001) and low Ki67 < 15% (HR = 2.382, p = 0.012) had higher relative risk of positive resection margins. In multivariate analysis, breast density of grade 4 (HR 1.700, p = 0.049), DCIS component on pathology (HR 4.747, p = 0.001), size discrepancy between breast MRI and ultrasonography > 0.5 cm (HR = 3.239, p < 0.0001) and non-triple negative breast cancer (HR 5.872, p = 0.041) showed higher risk of positive resection margin. 5-year Ipsilateral Breast Tumor Recurrence (IBTR) free survival rate was 99.2% in clear resection margins and 95.2% in positive resection margins after re-excision or mastectomy (p < 0.0001). All recurrences were observed within 3 years after first operation.

Conclusion: Breast density of grade 4 on mammography, DCIS and invasive cancer with DCIS component, size discrepancy more than 0.5cm between breast MRI and ultrasonography and non-triple negative breast cancer could be predictors for surgical resection margin status in breast-conserving surgery.

PO04-40

PHASE I STUDY WEEKLY PACLITAXEL COMBINING WITH GEMCITABINE FOR METASTATAIC BREAST CANCER PATIENTS

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Background/Purpose: Phase I study weekly paclitaxel combining with gemcitabine for metastatic breast cancer patients

Methods: Paclitaxel was administered weekly at 80 mg/m² and gemcitabine was 1,000 mg/m² (level 1)/1,250 mg/m² (level 2) at day1, 8 repeated 21 days according to the protocol approved by the Institutional review board of the Tokai University. A written informed consent was obtained from all patients. Six patients having a median age of 59 years (range, 35-75) were enrolled in level 1. All patients were hormone receptor-positive and HER2 negative (2 + cases were negative FISH). And three patients having a median age of 45 years (range, 39-60) were treated in level 2. Two patients were hormone receptor-positive, one was negative. One patient was HER2 positive, two were negative,

Results: In level 1 dose, the most frequent adverse events were neutropenia, leucocytopenia, anemia, thrombocytopenia and liver dysfunction. The severity of neutropenia was grade 1 in two patients (33%), grade 2 (17%) and grade 4 (17%) in one patient respectively. Thrombocytopenia was grade 1 in all patients (100%). The non-hematological toxicities were mild. All of these adverse events except neurotoxicity were reversible after 1-week withdrawal of chemotherapy. None of the patients required dose reduction or granulocyte colony-stimulating factor or had fever. We determined the adverse events were well tolerable in level 1 and migrated to next level 2.

Conclusion: A combination of weekly paclitaxel and gemcitabine can be safely administered 80 mg/m² and 1,000 mg/m². Additional cases in level 2 and more detail data would be shown at conference.

PO04-41

BREAST CONSERVING SURGERY AND SENTINEL LYMPH NODE BIOPSY UNDER LOCAL ANESTHESIA FOR EARLY BREAST CANCER

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Background/Purpose: In the current of less invasive surgery, breast conserving surgery and sentinel node biopsy has become the standard operation for early breast cancer. We have been undergoing this operation under local anesthesia to the patients who hope short-term admission or who dose not appropriate for general anesthesia due to their complications. Herein, we report our experience of breast conserving surgery and sentinel node biopsy under local anesthesia.

Methods: In the current of less invasive surgery, breast conserving surgery and sentinel node biopsy has become the standard operation for early breast cancer. We have been undergoing this operation under local anesthesia to the patients who hope short-term admission or who dose not appropriate for general anesthesia due to their complications. Herein, we report our experience of breast conserving surgery and sentinel node biopsy under local anesthesia.

Results: We could perform the operation under local anesthesia in all 42 patients, and no patient converted to general anesthesia. Two patients had sentinel lymph nodes metastasis. Surgical stumps were positive in 14 patients (33.3%). Ten Gray of boost irradiation toward the tumor bed was added to the conventional breast irradiation for these patients. Any serious complication associated with surgery occurred.

Conclusion: Breast conserving surgery and sentinel node biopsy can perform under local anesthesia safely for early breast cancer. This procedure contributes to shortening of hospitalization and saving medical resources without deceasing quality of treatment.

PO04-42

EXAMINATION OF THE SENTINEL LYMPH NODES BY MOLECULAR BIOLOGICAL AND CYTOLOGICAL TECHNIQUE DURING BREAST CANCER SURGERY

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Background/Purpose: We started to use One Step Nucleic acid Amplification (OSNA) in addition to cytological technique for sentinel lymph node examination during breast cancer surgery from July 2010. OSNA should provide higher sensitivity in diagnosing metastasis in lymph node because it detects CK19 mRNA of cancer cell. Therefore the combination use of these two techniques would give better confirmation if there is metastasis or not in the sentinel lymph node. Here we evaluate the usefulness of the combination in our cases.

Methods: We analyzed 89 cases in which we used both techniques for examination first by stamping every 2 mm surface of the dissected lymph node to glass slide then performed OSNA using the whole lymph node. In OSNA less than 250 copies/μL, and judged to be 1+ with 250-5,000 copies/μL was regarded as negative, 250-5,000 copies/μL was 1+, and over 5,000 copies/μL was 2+.

Results: Three cases showed discrepancy between two techniques (3.4%). All were positive in OSNA but negative in cytology. Both positive in OSNA and cytology was in 15 and both negative in OSNA and cytology was in 71 cases.

Conclusion: OSNA possesses a great advantage in detecting metastatic cancer cell in lymph node because the whole node is subjected to the examination while cytology subjected every 2 mm surface of the node. OSNA also possesses disadvantage because it may miss CK19 negative cancer cell. So the combination of these two technique for detection of cancer metastasis in lymph node would provide higher fidelity in the sentinel lymph node examination during breast cancer surgery.

PO04-43

THE PROGNOSIS FOR BREAST CANCER AFTER NEOADUVANT THERAPY; USING THE COMBINATION OF CLINICAL AND PATHOLOGIC PARAMETERS

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Background/Purpose: It is difficult to determine the prognosis of patients with neoadjuvant therapy, especially when they achieve less than a pathologic completion response from therapy. We studied that the outcomes for breast cancer patients treated with neoadjuvant therapy using the score system according combination of clinical and pathologic parameters

Methods: From 2000 to 2010, 306 patients treated with neoadjuvant chemotherapy for breast cancer in ASAN Medical Center were included. Clinical and pathologic characteristics and patients outcomes were investigated, retrospectively. America Joint Committee on Cancer (AJCC) clinical and pathologic staging parameters and biologic tumor markers were employed to devise the scoring system.

Results: Median follow up was 23 months. Two scoring systems, based on summing binary indicators for clinical substages ≥ IIB and ≥ IIIB, pathologic substages ≥ ypIIA and ≥ ypIIIC, negative estrogen receptor (ER) status, were devised to predict patient outcomes. When we applied the score with combination of clinical stage and pathologic stage, patients were more refined prognosis results according subgroups. And inclusion of ER status to combination of clinical stage and pathologic stage score provided additional prognostic value

Conclusion: Combination clinical, pathologic and biologic factors allowed for refining patients prognosis iver that of either AJCC clinical stage or pathologic stage alone.

PO05-01

SUPPLEMENTARY TOUCH IMPRINT CYTOLOGY OF THE CORE NEEDLE BIOPSIED SPECIMEN IMPROVED DIAGNOSTIC ACCURACY OF THE BREAST CANCER

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Background/Purpose: Recently, therapies targeting the biological characteristics of individual cancers have become available according to the markers indicating its molecular biological mechanisms. Core needle biopsy (CNB) is widely conducted not only to diagnose, but also to determine therapeutic strategy of breast cancer. Although its diagnostic accuracy has already become acceptably high level, false-negative results have occasionally been encountered.

Methods: The results of supplementary imprint cytology (SIC) underwent coincided with CNB in 1,114 patients who were suspected to have breast cancer was retrospectively reviewed. The feasibility and clinical usefulness of SIC assisted diagnosis was analyzed.

Results: Five-hundred sixty-seven cases were diagnosed as not malignant by CNB alone. Twenty of 567 cases (1.8%) were suspected malignant by cytological review of SIC, and 18 of them were confirmed to have breast cancer by additional biopsy. The combination of CNB with SIC accomplished a sensitivity of 100% (567/567) and the specificity of 99.6% (545/547). Small lesion, and large noninvasive- or scirrhous-type carcinomas were the common features of the CNB-negative/SIC-positive cases.

Conclusion: Supplementary imprint cytodiagnosis is a simple and easy procedure to assist the pathological diagnosis of breast cancer by CNB and, therefore, serves as a possible novel standard application.

PO05-03

DIAGNOSTIC VALUE OF PREOPERATIVE SONOGRAPHIC EVALUATION FOR AXILLARY LYMPH NODE METASTASES IN BREAST CANCER PATIENTS

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Background/Purpose: The aim of this study was evaluate predictive value of preoperative sonography for the evaluation of axillary lymph node metastases in breast cancer patients.

Methods: The study included 226 patients who underwent curative surgery from January 2008 to December 2010 at Inje University Sanggye Paik Hospital. We analyzed preoperative sonographic findings of axillary lymph nodes and compared the finding with postoperative histologic results of axillary lymph nodes evaluation.

Results: When we compared preoperative sonographic evaluation of metastatic lymph node with final histological results, the sensitivity of sonographic evaluation was 81.3% and specificity was 77.5%. False positive rate was 10.7% and false negative rate was 35.8%. The accuracy of preoperative sonographic evaluation of lymph node metastasis was 78.7%. Primary tumor size was the only significant predictive factor for lymph node metastasis on multivariate analysis.

Conclusion: preoperative sonographic evaluation of axillary lymph node had limited value with moderate accuracy. High false-negative rate of preoperative sonography indicates that preoperative sonography cannot replace intraoperative sentinel node evaluation at this stage.

PO05-04

CIRCULATING TUMOR CELLS IN PRIMARY AND METASTATIC BREAST CANCER PATIENTS

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Background/Purpose: Circulating tumor cells (CTCs) are isolated tumor cells disseminated from the site of disease in metastatic and/or primary cancers that can be identified and measured in the peripheral blood of patients.

Methods: Blood (7.5 mL) was collected from patients with stage II/III breast cancer who received neoadjuvant chemotherapy (NAC) or those with metastatic breast cancer (MBC) or recurrent breast cancer (REC). CTC levels were determined in 64 patients with stage II or III breast cancer before and after chemotherapy. CTCs at the beginning of chemotherapy were evaluated in 11 MBC and 25 REC.

Results: Only 2 of 64 (3.1%) stage II or III breast cancer patients showed 5 or more CTCs. One or more CTCs were detected in 12 (18.8%) of 64 operable patients before NAC, and CTCs disappeared after NAC in all patients. No difference in disease-free survival (DFS) was seen between patients with no CTCs and those with one or more CTCs. 5 or more CTCs were detected in 9 of 11 MBC and 17 of 25 REC. MBC and REC had a significantly more CTCs than stage II and III breast cancer. MBC patients with 5 or more CTCs showed a trend of a worse overall survival compared with those with 4 or less CTCs.

Conclusion: CTCs in operable breast cancer are less than MBC or REC. REC with 5 or more CTCs showed a poor prognosis.

PO05-05

THE POTENTIAL OF CANCER NANOTECHNOLOGY FOR DIAGNOSIS AND THERAPY OF BREAST CANCER

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Background/Purpose: Nanotechnology is the exciting field focused on man-made materials in the size range of 1-100 nanometers (nm). Nanoparticles are on the scale of many cellular-level processes and hence are attractive for targeting breast cancer (BC). Our group has recently developed Gold Speckled Silica nanoparticles (GSS) as multi-modal contrast agents for fluorescence, magnetic resonance and photoacoustic tomographic (PAT) imaging. The near infrared (NIR) optical absorption property of these particles makes them potentially useful for therapeutic applications such as thermal ablation of tumors.

Methods: GSS or saline (as control) were injected intratumorally in breast cancer mouse models. In vivo imaging was performed using PAT and ablation was achieved by exposure to near NIR laser (500 mW, 10min). Tumor ablation was determined by histologic analysis to assess the distribution and extent of tumor ablation, 24 hours following photothermal ablation.

Results: Following intratumoral injection of GSS, particles could be clearly imaged with PAT. Histological analysis showed significant photothermal tumor ablation in treated tumors after illumination with NIR light that was not seen in control treated tumors.

Conclusion: Evolving bio-nanotechnologies such as targeted GSS, nanoshells, and nanotubes promise to enhance the early detection and non-invasive diagnosis of BC. These safe technologies would offer higher specificity and enable higher compliance compared to conventional diagnosis strategies. Further, these new nanotechnologies could also serve as platforms for treating BC. Significant ongoing investment will be required if these new, emerging nanotechnologies are to realize their transformative potential for reducing the persistent burdens of BC.

PO05-08

ADDITIONAL LESION FOUND IN PREOPERATIVE BREAST MRI OF NEWLY DIAGNOSED BREAST CANCER

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Background/Purpose: With increased used of preoperative breast MRI in newly diagnosed breast cancer, due to its low specificity, additional lesion found has become an issue questioning the role of routine preoperative use. In this study we ought to analyze the characteristics of the additional lesion and to evaluate the clinicopathological factors associated with having additional malignancy.

Methods: We retrospectively reviewed 2491 patients who undergone surgery due to breast cancer in Seoul National University Hospital between Jan 2006 and Dec 2010. Patients undergone neoadjuvant chemotherapy or excision with initial sonography in other center were excluded and total 1068 were analyzed. The association between the clinicopathological factors and additional malignancy were evaluated. Accuracy was estimated regarding cancer yield, positive predictive value (PPV).

Results: Mean age was 50.9 years (21-85). Overall detection rate of additional lesion was 26.2% (280/1,068). Mean size of additional lesion was 9.8 mm (3-51). Additional lesion consist of 35.4% (99/280) C4 or higher, 62.1% (174/280) below C4, 2.5% (7/280) C0. One hundred patients undergone surgery and 19.3% (54/280) benign, 1.1% (3/280) atypical ductal hyperplasia, 4.6% (13/280) *in situ* carcinoma, 6.8% (19/280) invasive carcinoma and 3.9% (11/280) unknown lesions were found. Cancer yield was 2.99% (32/1,068) with PPV 39.0% (31/82). Breast density nor size, lymph node status, immunohistochemistry results of the primary cancer didn't show significance ($p = 0.705$, 0.381, 0.973, 0.375). Age, primary lesion with lobular component (Invasive lobular carcioma or mixed Invasive ductal carcioma with Invasive lobular carcioma) or low grade carcinoma showed significancy in both univariate ($p = 0.022$, 0.019, 0.022) and multivariate analysis(HR 0.95, $p = 0.014$), (HR 0.39, $p = 0.039$), (HR 5.66, $p = 0.035$).

Conclusion: Preoperative breast MRI should be considered in young age when primary lesion is low grade carcinoma with lobular component.

Poster Discussion

PO05-09

PREDICTING BREAST CANCER RECURRENCE FOLLOWING BREAST-CONSERVING THERAPY: BACKGROUND PARENCHYMAL ENHANCEMENT AROUND THE TUMOR ON PREOPERATIVE MRI

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Background/Purpose: To investigate which MRI and histopathologic features may be related to local recurrence in women treated with breast conserving therapy (BCT).

Methods: Between January 2005 and December 2010, of the 4911 breast cancer patients receiving BCT, 28 (0.6%) women were found to have local recurrence at a mean of 33.9 month follow-up (range 3-64 months). Fifty consecutive breast cancer patients who had no recurrent cancer at a mean of 63.6 month follow-up (range 61-68 months) were selected as a control group. Between the recurrence group and no recurrence group, there were no differences in mean patient age, stage, and histologic type. MRI features (amount of background parenchymal enhancement, morphology, kinetic features of the tumor, and distance to chest wall) and histopathologic features were compared between the two groups.

Results: Recurrence group showed greater enhancement of the parenchyma around the tumor at both early (91.1 ± 97.1 vs.56.6 ± 24.5, p = 0.019) and delayed phases of MRI (242.7 ± 305.9 vs. 96.8 ± 47.8, p = 0.001) than the no recurrence group. Recurrence group had higher nuclear grade [grade 1, 0% (0/24) vs. 4.3% (2/47), grade 2, 33.3% (8/24) vs. 61.7% (29/47), grade 3,66.7% (16/24) vs. 34.0% (16/47); p = 0.022] and more negative ER [negative 64.3% (18/28) vs. 28.0% (14/50), positive 35.7% (10/28) vs. 72.0% (36/50); p = 0.004] than the no recurrence group. No differences were found in other imaging and histopathologic features.

Conclusion: Stronger enhancement of parenchyma around the tumor is related to local recurrence in breast cancer patients treated with BCT in addition to previously established histopathologic prognostic factors.

PO05-10

PREDICTABLE CLINICAL FACTORS OF AXILLARY LYMPH NODE METASTASIS IN T1 BREAST CANCER

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Background/Purpose: Axillary lymph node metastasis (ALNM) is the important prognostic factors in breast cancer. After sentinel lymph node biopsy was introduced, it has replaced standard axillary lymph node dissection for staging and local control in patients with clinically negative lymph nodes. However, recently, a few studies reported that some of the patients who had positive sentinel nodes were treated safely without further axillary lymph node dissection. Although many studies on factors involved in ALNM were published from the past, but most of these factors can be identified only through pathologic reports and thus cannot help preoperatively. So we planned the studies to identify the predictive clinical factors of ALNM in T1 breast cancer.

Methods: We reviewed the medical record of T1 invasive ductal carcinoma patients who had been operated between January 2000 and December 2009.

Results: Of the 248 patients, 65 (26.2%) patients had axillary lymph node metastasis (N1 = 46, N2 = 8, and N3 = 11). The patients who did breast feeding for less than three month showed higher frequency of ALNM (42.9% vs. 21.4%, $p = 0.003$). The patient's age and tumor size were not related, but multiple cancer and suspicious lymph node on image work-up were identified to significant predictable factors (44.8% vs. 25%, $p = 0.023$ and 69.2% vs. 16.1%, $p < 0.001$). Also, the patients who were underweight (BMI < 18.5 kg/m^2) or obese (BMI ≥ 30 kg/m^2) in category of BMI showed higher frequency of ALNM ($p = 0.032$).

Conclusion: If we identify the predictable clinical factors of ALNM, it will be helpful to the treatment of the early breast cancer with more less invasive modalities.

Poster Discussion

PO05-11

CORRELATION BETWEEN MAMMOGRAPHIC BREAST DENSITY, BACKGROUND ENHANCEMENT IN MR MAMMOGRAPHY AND QUANTITATIVE BACKGROUND FDG UPTAKE ON PEM

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Background/Purpose: To investigate the influence of mammographic breast density on background enhancement in MR mammography and quantitative background FDG uptake in normal glandular breast tissue.

Methods: A total of 100 patients (mean age, 52.16 years) with newly diagnosed invasive ductal carcinoma were included in this retrospective study. The mammograms were retrospectively reviewed for overall breast density according to the four-point scale (I-IV) of the BI-RADS classification. The MR mammographies were retrospectively reviewed and background enhancement was classified as minimal, mild, moderate, or marked. The background mean FDG uptake value (PUV mean) on Positron Emission Mammography (PEM) was obtained by drawing a user-defined Region of Interest (ROI) in a normal area of the breast that was representative of mixed glandular and fatty back-ground tissue.

Results: Of the 100 mammograms, 9% showed almost entirely fatty, 54% showed scattered fibroglandular, 27% showed heterogeneously dense, 10% showed extremely dense pattern. The average age of patients with fatty breasts was significantly higher than that of patients with dense breasts ($p < 0.001$). And background 18F-FDG uptake on PEM (PUV mean) decreases as patient's age increases. Patients with dense breasts exhibited a significantly higher proportion of moderate or marked background enhancement at 37.83% compared with those classified as fatty breasts at 11.11% ($p = 0.002$).

Conclusion: Background 18F-FDG uptake on PEM (PUV mean) significantly increases as age decreases and breast density increases. Patients with heterogeneously or extremely dense breasts exhibited a significantly higher proportion of moderate and marked background parenchymal enhancement on MR mammography compared with those classified as almost entirely fatty and scattered fibroglandular density.

PO05-12

DISCREPANCY BETWEEN RADIOLOGICAL AND PATHOLOGICAL SIZE OF BREAST CANCER AFTER VACUUM ASSISTED BREAST BIOPSY

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Background/Purpose: Assessing the pathological size of tumor removed by vacuum assisted breast biopsy (VABB) is not convenient due to multiple fragmentations. Moreover VABB can remove a fairly large volume so the actual pathological measurement of breast cancer tumor size after VABB can be downstaged. Our study aimed to compare the radiological size of breast cancers on ultrasonography (USG) with the pathological specimen size after VABB.

Methods: 5,010 patients underwent real-time ultrasound guided VABB, of whom 248 with malignant lesion received subsequent surgery. 168 patients with invasive carcinoma were enrolled and 80 patients with *in situ* carcinoma were excluded from the study. All enrolled patients (n = 168) were divided into subgroups according to its USG and pathological specimen size.

Results: Among 108 (65.5%) patients with pT1, there was a discrepancy between clinical and pathological size in 95 (88.0%) patients. USG oversized in 71 (65.7%) patients, downsized in 24 (22.3%) patients, equaled in 13 (12.0%) patients. While in 60 (35.7%) patients with pathological T size greater or equal than T2, there was a discrepancy between clinical and pathological size in 50 (3.4%) patients. USG oversized in 28 (46.7%) patients, downsized in 22 (36.7%) patients, equaled in 10 (16.6%) patients.

Conclusion: Tumor size discrepancy between ultrasonography and pathological specimen measurement after VABB existed considerably when preoperative USG tumor size was less than or equal to 2 cm. This discrepancy can mislead to underestimate the actual cancer staging and eventually omitting crucial adjuvant chemotherapy. For some patients following VABB, preoperative ultrasonography tumor size can be useful for clinical staging when there is insufficient residual tumor left on postoperative pathological specimen.

Table 1. Clinicopathological characteristics of breast cancer patients (n=168).

Characteristics	No. of patients(%)
Mean Age (yr): 46±10.89, Range 22-76	
BI-RADS* Classification of ultrasound	
Category 3	6 (3.6)
Category 4a	29 (17.3)
Category 4b	31 (18.4)
Category 4c	42 (25.0)
Category 5	60 (35.7)
pT stage	
pT1	108 (64.2)
pT2	53 (31.6)
pT3	6 (3.6)
pT4	1 (0.6)
N stage	
N0	102 (60.7)
N1	38 (22.6)
N2	13 (7.8)
N3	15 (8.9)
Stage	
I	78 (46.4)
IIA	42 (25.0)
IIB	22 (13.1)
IIIA	13 (7.7)
IIIB	3 (1.8)
IIIC	8 (4.8)
IV	2 (1.2)
Operation**	
TM	76 (45.2)
BCS	92 (54.8)
Pathology***	
IDC	150 (89.3)
ILC	7 (4.1)
IMuC	4 (2.4)
ITC	4 (2.4)
IMeC	2 (1.2)
IPC	1 (0.6)

BI-RADS*: breast imaging reporting and data system; Operation**: TM; total mastectomy, BCS; breast conserving surgery; Pathology***: IDC; invasive ductal carcinoma, ILC; invasive lobular carcinoma, IMuC; invasive mucinous carcinoma, ITC; invasive tubular carcinoma, IMeC; invasive medullary carcinoma, IPC; invasive papillary carcinoma.

Table 1.

Table 2. Comparison of USG and pathologic specimen according to its size.

USG size	Pathologic size compared to USG size		
	Lesser	Equal	Larger
≤1cm: Group I (n=17)	4(23.5%)	4(23.5%)	9(53.0%)
>1cm~≤2cm: Group II (n=73)	44(60.3%)	9(12.3%)	20(27.4%)
2cm>: Group III (n=78)	51(65.4%)	10(12.8%)	17(21.8%)

pT size	Pathologic size compared to USG size		
	Lesser	Equal	Larger
pT1 (n=108)	71(65.7%)	13(12.0%)	24(22.3%)
>pT2 (n=60)	28(46.7%)	10(16.6%)	22(36.7%)

Table 2.

PO05-13

DIFFERENCES IN ACCURACY AND UNDERESTIMATION RATES FOR 14- VERSUS 16-GAUGE CORE NEEDLE BIOPSIES IN ULTRASOUND-DETECTABLE BREAST LESIONS

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Background/Purpose: Core needle biopsy (CNB) was widely used in the diagnosis of ultrasound detectable breast lesion; however, rare information was available comparing the diagnostic differences between 14-gauge and 16-gauge ultrasound-guided large-core biopsies.

Methods: A retrospective analysis of patients receiving CNB during the period of January 2001 to December 2007 in Changhua Christian Hospital was conducted. Data collected included patient's age, gender, number of samples per CNB procedure, lesion size, preoperative ultrasound diagnosis, and final pathologic report. The accuracy and rate of disease underestimation for 14-gauge versus 16-gauge breast needle core biopsies were made with CNB results compared with pathology of open surgical biopsy (OSB).

Results: A total of 1,024 paired CNB and OSB results were obtained from 1,732 CNB procedures in 1,630 patients. Our CNB results reached 92.9% sensitivity, 99.7% specificity, 5.96% underestimation, and 94.8% accuracy rate. Compared between 14- and 16- gauge needles, there was no difference in sensitivity (94.5% vs. 91.9%, $p = 0.17$), or specificity (100% vs. 99.1%, $p = 0.38$). However, better overall accuracy (96.6% vs. 93.3%, $p = 0.02$), less underestimation (2.56% vs. 8.84%, $p < 0.001$), and a lower false negative rate (6.5% vs. 3.4%, $p = 0.02$) were found for the 14-gauge needle as compared with the 16-gauge. The only false positive case was found with the use of the 16-gauge needle.

Conclusion: In terms of accuracy and underestimation rate, the 14-gauge is preferred over the 16-gauge needle in ultrasound-guided biopsies.

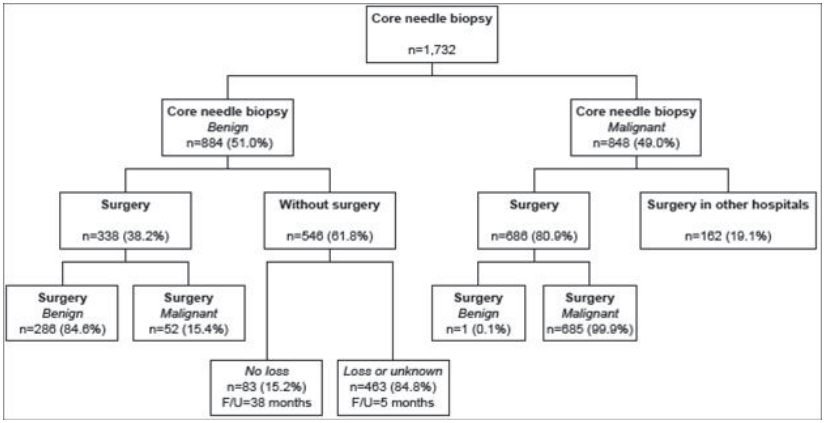

Fig. 1

Table 4. Comparison of sensitivity, specificity, accuracy and underestimation rate between 14- and 16-gauge core needles

		CNB		
	Total (n=1024)	14-gauge needle (n=470)	16-gauge needle (n=554)	P value
Sensitivity (%)	685/737 (92.9)	277 /293 (94.5)	408 /444 (91.9)	0.17
Specificity (%)	286/287 (99.7)	177/177 (100)	109/110 (99.1)	0.38
Accuracy				
Yes (%)	971/1 024 (94.8)	454/470 (96.6)	517/554 (93.3)	0.02
No (%)	53/1 024 (5.2)	16/470 (3.4)	37/554 (6.7)	
Underestimation				
Yes (%)	61/1024 (6.0)	12/470 (2.6)	49/554 (8.8)	<0.0001
No (%)	962/1024 (94.0)	457/470 (97.4)	505/554 (91.2)	
False negative				
Yes (%)	52/1024 (5.1)	16/470 (3.4)	36/554 (6.5)	0.02
No (%)	972/1024 (94.9)	454/470 (96.6)	518/554 (93.5)	
False positive				
Yes (%)	1/1024 (0.1)	0/470 (0)	1/554 (0.2)	–
No (%)	1 023/1024 (99.9)	470/470 (100)	553/554 (99.8)	

Table 1.

PO05-14

ANALYSIS OF CLINICOPATHOLOGIC FACTORS CORRELATED WITH INVASIVENESS IN DUCTAL CARCINOMA *IN SITU*

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Background/Purpose: Ductal carcinoma *in situ* (DCIS) coexisting invasion is commonly seen and no consensus on any marker capable of discriminating this subgroup has been reached yet. We retrospectively examined the clinicopathologic factors and immunophenotypes between pure DCIS and DCIS coexisting invasion patients.

Methods: A total of 151 patients with preoperative Biopsy-proven DCIS without obvious evidence of Invasive ductal carcinoma (IDC) were reviewed from April 2005 to May 2011. The presence of IDC, clinicopathologic factors of DCIS and IDC, radiologic findings and their estrogen receptor (ER), progesterone receptor (PR), and HER2 phenotypes were evaluated.

Results: Ninety-four patients had pure DCIS, and 57 patients had DCIS with invasion in pathologic reports. Malignant calcification in mammography (MMG) ($p = 0.002$), satellite nodule in ultrasonography (USG) ($p = 0.023$), ER positivity ($p = 0.046$), PR positivity ($p = 0.009$) were correlated with invasive cancer. HER-2 positivity did not show the relationship ($p = 0.215$) , and the luminal A, B, basal & HER-2 subtypes showed no difference between the two groups. Only malignant calcification in MMG has statistical significance in the multivariate logistic regression analyses (odds ratio 2.32 95% CI 1.15-4.68).

Conclusion: Malignant calcification may be used to identify DCIS patients at higher risk of harboring or potentially developing IBC. ER/PR/HER2 phenotypes in DCIS may not have a potential benefit in forecasting IDC in patients with DCIS.

PO05-15

PROGNOSIS OF INTRAOPERATIVE, FALSE-NEGATIVE SENTINEL LYMPH NODE BIOPSIES IN BREAST CANCER PATIENTS

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Background/Purpose: Axillary lymph node dissection (ALND) has been a standard treatment for breast cancer patients with positive sentinel lymph nodes (SLNs). However, over 50% of patients with positive SLNs had only positive SLN and, in theory, did not need ALND. The main objective of the current study was to determine the prognosis of patients with an intraoperative, false-negative sentinel lymph node biopsy (SLNB).

Methods: Total 516 women who had unilateral invasive breast cancer with clinically negative nodes or nodes suspicious for metastasis, were intraoperatively diagnosed as having negative SLNs, and did not undergo an immediate ALND. Of these 516 women, 53 (10.3%) were postoperatively diagnosed as having positive SLNs, which classifies them as having an intraoperative, false-negative SLNB. Patient and tumor characteristics, treatment methods, and the prognoses of these patients were investigated and compared with the remaining 463 patients who were negative for SLNB.

Results: Of the 53 patients with intraoperative, false- negative SLNB, none underwent a further ALND. With a median follow-up period of 31.0 months, seven of these patients exhibited recurrence in the locoregional area and 2 death. In univariate analyses, the hazard ratios for recurrence free survival in the intra-operative false negative SLNB compared with that in the negative SLNB was 3.49 ($p = 0.0048$; 95% CI, 1.46-8.32).

Conclusion: It is currently unclear whether ALND can be avoided in most patients with breast cancer with intraoperative, false-negative SLNB. However, patients with pN0 (i+) or with pN1mi had other poor prognostic factors and needed to receive more aggressive therapy.

PO05-16

CLINICOPATHOLOGIC FACTORS FOR PREDICTING NON-SENTINEL LYMPH NODE METASTASIS FOR SENTINEL LYMPH NODE POSITIVE BREAST CANCER PATIENTS

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Background/Purpose: Completion axillary dissection is a standard treatment for the sentinel lymph node (SLN) positive breast cancer patients. However, over 50-65% of these patients do not have additional LNs metastases. So some studies suggested predictor factors for non sentinel positive lymph node (NSLN) in SLN positive cases. But, these are based on pathologic findings, which were mostly informed after surgery. We performed this study to analyzed clinicopathological factors which we can know before or during the surgery for predicting NSLN status in SLN positive breast cancer.

Methods: During the period between April 2001 and May 2011, 513 patients underwent breast cancer surgery and SLN biopsy with or without completion axillary dissection. Among these, 83 patients were enrolled in this study. Inclusion criteria were as follows: 1) patient with four or more than four SLNs, 2) patient with metastatic SLN, and 3) patients who underwent completion axillary dissection. We analyzed the tumor type, hormonal receptor status, tumor location, histologic grade, nuclear grade, metastatic SLN ratio (metastatic SLN/harvested SLN), tumor size and mutifocality/muticentricity. Cut off value of tumor size, and metastatic SLN ratio was also evaluated.

Results: Among the various factors, tumor size ($p = 0.023$), multifocality/muticentricity ($p = 0.019$) and SLN ratio ($p < 0.001$) were significantly related with NSLN metastasis. The best cut off value of tumor size and metastatic SLN ratio were 1.81cm (AUC: 0.65) and 0.33 (AUC: 0.75), respectively.

Conclusion: We think that tumor size, multifocality/multicentricity and SLN ratio could be predictive factors for NSLN metastasis. However, more lots of studies for this should be needed.

PO05-17

RELIABILITY OF ONE LEVEL INTRAOPERATIVE FROZEN SECTION DIAGNOSIS IN DETERMINING THE STATUS OF SENTINEL LYMPH NODES INTRAOPERATIVELY IN BREAST CANCER

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Background/Purpose: Intraoperative frozen section (FS) diagnosis of SLN can be used to detect metastasis and also avoid unnecessary axillary clearance (AC). However, optimal technique for rapid SLN assessment has yet to be determined. This study aims to outline the usefulness of one level intraoperative FS evaluation of SLNs in breast cancer patients.

Methods: We reviewed the results of 113 breast cancer patients who underwent intraoperative sentinel lymph node (SLN) biopsy between January 2010 and May 2011. FS procedure using a 6 micron thick single section (one level) stained with hematoxylin and eosin (HE) was employed in the SLN analysis. Patient with positive SLNs based on FS diagnosis proceeded to AC. The remaining frozen tissues were sectioned at one level 3 micron thick on subsequent day and diagnosed using HE without immunohistochemical (IHC) staining.

Results: One level FS correctly identified 18 out of 21 metastases with a sensitivity of 86%, specificity of 100%, negative predictive value 97.8% when compared with one level final histopathology evaluation. Accuracy and positive predictive value were 97.3% and 100%. The false negative rate (FNR) in this study was 14.3%, comparable to the 16% FNR in one level technique demonstrated in current literature.

Conclusion: We conclude that the sensitivity and specificity of one level intraoperative FS evaluation of SLN biopsy matche the higher end percentages reported in literature. Single section HE analysis of SLN without IHC staining is rapid, has high positive and negative predictive values, provided the same surface is used in the final histological evidence. This procedure could be applied in many institutions.

PO05-18

MANAGEMENT OF A FAILURE OF SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER

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Background/Purpose: Sentinel lymph node (SLN) biopsy for breast cancer is common in clinical practice. Highly detection rate was reported. However, in a few case SLN biopsy was not succeeded. We examined the cases that had not been detected SLN.

Methods: From May 2004 to August 2010, 500 cases were performed SLN biopsy by the combination of radioisotope (RI, 99mTc-tin colloid) and dye (Indocyanine Green). Clinical Node status was evaluated by CT and Ultrasonography. RI injection was done in the afternoon previous day of operation at intradermal areola. Scintigraphy was performed 1-2 hours later. Dye injection was done just before starting operation at the same place.

Results: Four cases of 500 patients (0.8%) were not succeeded by the combination of RI and dye methods. All four cases were not seen hot lymph node (LN) by scitigraphy. Two were age 60's and the others were age 80's. High BMI case is only one patient (60's), others were normal BMI. Tumor size is 15-35mm, one was DCIS. Two 80's patients and one high BMI patients were done axillary LN sampling as informed before operation. The other was performed axillary LN dissection.

Conclusion: In this analysis, SLN detectability seemed to be concerned the age not BMI. In aged or complicated patients, we would like to avoid axillary LN dissection. So, we should explain that whether axillary LN dissection or sampling will be done if the scintigraphy does not detect the hot LN in such a patients.

PO05-19

S-1 COMBINED WITH IRINOTECAN (CPT-11) AND TRASTUZUMAB FOR PATIENTS WITH HER2 POSITIVE ADVANCED/RECURRENT BREAST CANCER

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Background/Purpose: Irinotecan, S-1 and trastuzumab have been shown to be effective in patients with advanced/recurrent breast cancer and they have a considerable single-agent activity, respectively. We evaluated the combination of irinotecan (CPT-11), S-1 and trastuzumab chemotherapy for advanced or recurrent breast cancer.

Methods: All patients with histologically confirmed HER2 positive breast cancer with unresectable or metastatic diseases, measurable lesions, and no contraindication to chemotherapy were treated. Treatment included S-1 80 mg/m^2 orally, twice a day on days 3 to 7, 10 to 14, and 17 to 21 and CPT-11 60 mg/m^2 i.v. on day 1, 8, 15 with a 1-week interval, and trastuzumab 4 mg/kg (first time), 2 mg/kg (subsequent weekly) until disease progression or unacceptable toxicities.

Results: Eight patients were treated by this regimen so far. The median age was 52 years (range, 32-62). The overall response rate was 50.0%, including 1 CR, 3 PRs, 3 SDs, and PD. The clinical benefit rate was 87.5%. Commonly observed grade 3/4 adverse events were neutropenia (25% of patients), diarrhea (12.5%). There was no neutropenic fever or treatment-related death.

Conclusion: The combination of CPT-11 and S-1, trastuzumab appear to have well efficacy, manageable toxicity and is well tolerated in patients with HER2 positive advanced/recurrent breast cancer. Further studies of this combination are scheduled in a multicenter phase II study.

Poster Discussion

PO05-20

DUCTAL CARCINOMA *IN SITU* DETECTED BY SONOGRAPHY ALONE: RADIOLOGIC AND CLINICOPATHOLOGIC FEATURES

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Background/Purpose: To evaluate radiologic and clinicopathologic features of ductal carcinoma *in situ* (DCIS) detected by sonography (US) alone with negative on mammogram.

Methods: From October 2003 to May 2010, 18 patients with DCIS lesions detected by US alone were enrolled in the study. Clinical symptoms, such as palpable lump, nipple discharge, or pain, were recorded. Imaging findings were retrospectively analyzed by two radiologists with consensus according to BI-RADS lexicon and BI-RADS final assessment categories were recorded.

Results: Of the 18 patients, 6 patients were symptomatic and bloody nipple discharge with lump was the most common symptom (n = 4). Mammography showed dense parenchyma in 17 patients. On US, the most common finding was a mass (size range, 0.7-1.9 cm; mean, 1.0 cm) in 14 cases (77.8%), followed by ductal change in 3 (16.7%) and low echoic area in 1 (5.5%). Masses showed irregular shape in 9 cases (64.3%) and oval shape in 5 (35.7%). The margins were most commonly indistinct (n = 7). BI-RADS final assessment categorization was classified as category 3 in 1 (5.5%), 4a in 7 (38.9%), 4b in 8 (44.4%), and 4c in 2 (11%). Of the 18 DCIS lesions, 11 (61.1%) were classified as non-high nuclear grade and 7 (38.9%) as high grade. Comedonecrosis was seen in only three cases (16.7%).

Conclusion: Hypoechoic masses with indistinct margin, irregular shape, no posterior acoustic feature, parallel orientation, and abrupt interface were the most common finding in DCIS detected by US alone. These lesions can be misdiagnosed as benignity due to lack of typical malignant features.

PO05-22

THE HORMONE RECEPTOR, HER-2 AND MOLECULAR SUBTYPE STATUS OF INDIVIDUAL TUMOR FOCI IN MULTIFOCAL/MULTICENTRIC INVASIVE DUCTAL CARCINOMA OF BREAST

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Background/Purpose: Multifocal/multicentirc breast cancers are common. However, investigations of biomarkers such as ER, PR and HER-2 in the individual tumor foci of multifocal/multicentirc breast cancers were rare. This study was designed to evaluate the status of the hormone receptor, HER-2 and its molecular subtypes in the individual tumor foci of multifocal/multicentirc invasive ductal carcinoma (IDC) of breast and to identify the factors associated with the different phenotypes of individual tumor foci.

Methods: We performed immunohistochemical analyses of the estrogen receptor (ER), progesterone receptor (PR), cytokeratin 5/6, epidermal growth factor receptor and p53, and fluorescence *in situ* hybridization of HER-2, in the individual tumor foci of 65 cases of multifocal/multicentirc IDC and in the associated ductal carcinoma *in situ* (DCIS) components, using tissue microarrays.

Results: ER status differed in two (3%) of the 65 multifocal/multicentirc IDCs, PR status in seven (11%), HER-2 status in four (6%) and molecular subtypes in five (8%). The presence of different molecular subtypes in the invasive tumor foci was associated with differences in the histologic features of the tumors ($p = 0.005$), high histologic and nuclear grade ($p = 0.012$, $p = 0.021$, respectively), p53 overexpression ($p = 0.006$) and mixed molecular subtypes in the DCIS components ($p = 0.011$).

Poster Discussion

Conclusion: Multifocal/multicentirc IDCs usually have a single phenotype in terms of hormone receptor, HER-2 and molecular subtypes and, thus, immunohistochemical analyses of index tumor may be sufficient in routine practice. However, if multifocal/multicentirc IDCs are of high grade, of different histologic features, or of heterogeneous DCIS component, biomarkers are needed to be evaluated separately.

PO05-23

DETECTION OF CIRCULATING TUMOR CELLS IN PERIPHERAL BLOOD OF METASTATIC BREAST CANCER PATIENTS

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Background/Purpose: Circulating tumor cells (CTCs) are detected in peripheral blood of breast cancer patients, and they may play an important role as a prognostic and predictive marker. We conducted this study to determine the presence of CTCs with the EpiCAM and the clinical significance in treatment of metastatic breast cancer.

Methods: Thirty-eight MBC patients were enrolled. These patients were followed by assessing CTCs, imaging studies, and serum tumor markers. Blood samples were collected before starting a new treatment and at the treatment evaluation period (2-3 months after starting chemotherapy). The cutoff for CTC level was 5.

Results: At baseline, 12 of 38 patients (32%) had ≥ 5 CTCs per 7.5 mL of blood. At the evaluation period, 3 of 12 patients (22%) had ≥ 5 CTCs. The baseline CTC number did not contribute to determine their overall survival (OS); however, CTCs at the evaluation period were available to predict their OS ($p = 0.001$). In two cases, both CTCs and tumor markers were available as predictors of treatment efficacy. In two other cases, although alterations of tumor markers might not reflect disease condition, CTC alteration corresponded to their condition. One patient who had multiple skeletal metastases only, experienced a decrease in her CTCs in spite of tumor marker alteration.

Conclusion: We suggest that monitoring the number of CTCs may be helpful in predicting the efficacy of the treatment and the prognosis. CTCs might be especially useful with patients whose lesions are difficult to assess

PO05-24

ONE-STEP NUCLEIC ACID AMPLIFICATION ASSAY: ROUTINE INTRAOPERATIVE MOLECULAR ANALYSIS OF SENTINEL LYMPH NODE IN BREAST CANCER AT A PRIVATE CLINIC

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Background/Purpose: Detection of sentinel lymph node (SLN) metastasis in breast cancer is crucial for clinical stage evaluation and selection of axillary dissection. Quicker, easier and more accurate than histology, one-step nucleic acid amplification (OSNA) has been adopted as routine procedure for intraoperative SLN assessment in our clinic, enables us to detect metastases by quantitative analysis of cytokeratin 19 (CK19) mRNA in SLN in nearly half an hour. In this study, half of the SLN underwent histological examination, then both OSNA and histological results were compared.

Methods: For this study, surgically obtained 246 SLNs were bisected so that one half was used for OSNA assay to distinguish macrometastasis (++), micrometastasis (+), nonmetastasis (-). The central slice of the other half was examined histopathologically by H&E stain. The two results were then compared.

Results: Of 239 SLNs, excluding 7 cases due to OSNA-related machine error, positive or negative control error, OSNA assay detected more SLN metastases than histology (OSNA: 57 out of 239, i.e. 23.8%, vs. histology: 44 out of 239, i.e. 18.4%, $p = 0.0009$). Overall concordance with histology was 93.7% with 97.7% sensitivity and 92.8% specificity. Most of the 14 discordant cases involving negative histological results were OSNA (+) cases.

Conclusion: OSNA assay is more effective for detection of SLN metastasis than conventional histopathology using Hematoxylin and Eosin stain. In a private clinic, OSNA assay can allow accurate and rapid intraoperative SLN assessment.

PO05-25

COMPARISON OF MAMMOGRAPHIC BREAST DENSITY BETWEEN DUCTAL CARCINOMA *IN SITU* AND BENIGN BREAST DISEASE

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Background/Purpose: It is well known that high mammographic density is an independent risk factor of breast cancer. High mammographic density is also known to be a risk factor in incidence of benign breast diseases. But there are not enough studies about mammographic density of ductal carcinoma *in situ* (DCIS) and benign breast diseases (BBD). We compared mammographic density of DCIS and BBD and analyzed the differences.

Methods: We retrospectively reviewed mammogram of 345 patients with DCIS and 295 patients with BBD who had been operated in Asan Medical center. Mammographic density was assessed by computer assisted thresholding method, Cumulus™ 4, version 4.0. Craniocaudal view of unaffected breast was digitized for calculation of percentage density (PD).

Results: The mean PD of DCIS and BBD were 44.89% and 45.27%, respectively. There was no significant difference ($p = 0.79$). We categorized the patients by age (≥ 50 and < 50) in each group. Mean PD of DCIS and BBD in below 50 year-old groups were 52.92% and 49.58%, respectively. And those of above 50 year-old groups were 33.67% and 32.29%, respectively. In age group below 50 years old, DCIS has significantly ($p = 0.031$) higher mammographic density.

Conclusion: As shown in the result, mean values and distribution patterns of PD were similar between BBD and DCIS group. However, in the subgroup aged under 50, the DCIS group has significantly higher breast density than the BBD group. To find out clear relationship of mammographic density of DCIS and BBD group, we need more data and investigations in the future.

Poster Discussion

PO05-26

ROLES OF SENTINEL LYMPH NODE BIOPSY IN PATIENTS WITH BREAST DUCTAL CARCINOMA *IN SITU*

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Background/Purpose: To evaluate the roles of sentinel lymph node biopsy (SLNB) in patients with breast ductal carcinoma *in situ* (DCIS).

Methods: A database from 13 multi-centers of China Breast Cancer Clinical Study Group, that contained 237 patients with the diagnosis of breast DCIS and 88 patients with the diagnosis of breast ductal carcinoma *in situ* with micro-invasion (DCISM) who received SLNB from January 2002 to May 2011, was retrospectively analyzed.

Results: The sentinel lymph node (SLN) positive rate of 325 patients was 6.15%. Of 237 patients with DCIS, the positive rate was 3.8%, and the rate was significantly higher in patients with ultrasound diagnosed large tumors ($p = 0.038$) or those with high histological grade tumors ($p < 0.001$). Of 88 patients with DCISM, the rate was 12.5%, and it was significantly higher than that of patients with DCIS ($p = 0.004$). The younger patients with DCISM had a significantly higher risk of SLN metastasis ($p = 0.033$).

Conclusion: SLNB should be done in all DCISM patients and in those DCIS patients who received mastectomy, and could be avoided in those who received breast conserving surgery. However, SLNB should be recommended to patients who have high risks of harboring invasive components.

PO05-27

REAL-TIME 3-D VIRTUAL NAVIGATION FOR SENTINEL NODE BIOPSY

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Background/Purpose: Sentinel node biopsy (SNB) has become a new standard of care for early stage breast cancers. Two mapping method (blue dye and radioactive colloid) appears to be complementary, minimizing the false negative rate. But it is difficult to use radioactive tracer in most of Japanese institutes. For the improvement of success rate and safety of dye-guided procedure, we developed a new navigation technique.

Methods: Multi-detector row computed tomography (MD-CT) and CT lymphography (CT-LG) with iopamidol was performed for the SNB candidate. Images of MD-CT were analyzed by image processing software 'OsiriX'. OsiriX is an open-source software which anyone can download from website (http://www.osirix-viewer.com). OsiriX has been specifically designed for visualization of multidimensional images. We used 3D volume rendering images. At the time of surgery, volume rendering images of CT-LG ware superimposed directly on the patients' skin from projector which was connected to a personal computer in the operating room.

Results: We could see 'real-time' rendering images (from skin to organ by layer to layer) on the patient's body. By using CT-LG imaging data, we could recognize precise SLN location and could perform SNB safer and easier than before.

Conclusion: 3-D reconstruction MD-CT images of CT-LG were helpful to understand the anatomy of the axilla especially for resident and trainee, and 'real-time' virtual navigation made SLNB easier. This new technique does not need any expensive equipments and easily performed by surgeon. Ordinary personal computer and projector make it possible to demonstrate a new environment in surgical operation.

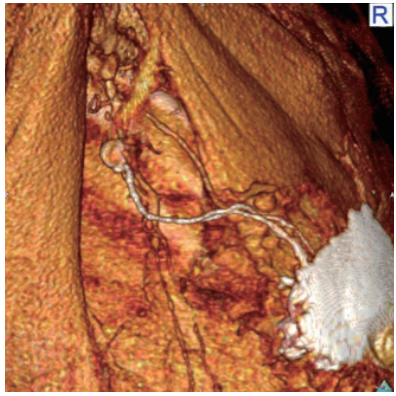

Fig. 1

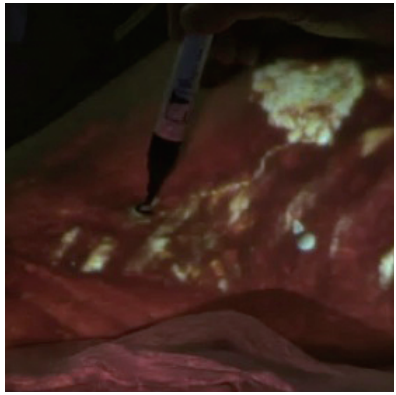

Fig. 2

PO05-28

DEVELOPMENT OF A CLINICAL PREDICTION MODEL FOR AXILLARY LYMPH NODE METASTASIS IN PRIMARY BREAST CANCER PATIENTS: A VALIDATION STUDY AND A LITERATURE REVIEW

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Background/Purpose: Prediction of axillary lymph node (AxLN) metastasis is a crucial issue in primary breast cancer management. Several clinical prediction models, i.e. scoring systems or nomograms, for AxLN metastasis have been reported. We developed a decision tree-based prediction model for AxLN metastasis using two modeling datasets from Japanese institutions. Our model showed accuracy with the area under the receiver operating characteristics curve (AUC) values 0.917 and 0.770 in the modeling datasets. The validation study was conducted using clinicopathological information from Korean breast cancer patients. We also reviewed published models to elucidate the problems in development and assessment of clinical prediction models.

Methods: The validation dataset consisted of 174 patients from Seoul National University Hospital who underwent sentinel lymph node biopsy. Published models to predict AxLN metastasis were identified from articles indexed between 2000 and 2011 in MEDLINE using the key words breast cancer and lymph node and prediction model or nomogram or scoring system.

Results: The validation study showed the robust predictive ability of our model (AUC 0.772). Eighteen published models were identified. The discrimination ability of our

Poster Discussion

model was comparable to the previous models. In the review, variability of the results of external validation studies was also demonstrated (AUC ranged from 0.58 to 0.86).

Conclusion: Our model showed the generalization capacity in the validation study using an independent dataset. However, the model requires more variables compared to the published models and the calibration could be improved. Combined use of our model and other models could provide more accurate prediction.

PO05-29

THE ROLE OF ULTRASOUND-GUIDED MAMMOTOME SECOND-BIOPSY FOR DETERMINING THE OPTIMAL EXCISION AREA OF BREAST CANCER SURGERY

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Background/Purpose: Preoperative imaging is accurate methods to diagnose the extent of breast cancer. However over- or under estimations cause over- or under-surgery. We assessed whether ultrasound-guided mammotome biopsy (US-MMT) is useful to make benign or malignancy of the suspicious lesions around the main tumor and to decide an adequate area of resection in patients with breast cancer.

Methods: Fifty-one women with primary breast cancer underwent US-MMT to the suspicious but undefined lesions around the main tumor for determining the presence of cancer spreading as a second biopsy. After surgery, the specimens were reviewed pathologically.

Results: US-MMT was performed for 70 lesions in 51 breast cancer patients. Twenty-three lesions were diagnosed as malignancy, 45 lesions as no malignancy, and 2 lesions as atypical lesion or lobular neoplasia. Based on these results, 37 patients (72.5%) were performed partial mastectomy (procedures were changed from total to partial mastectomy in 10 patients), 14 patients (27%) were performed total mastectomy (partial to total mastectomy in 6 patients). The area of excision was re-adjusted according the result of a second biopsy in 27 of 37 partial mastectomy cases. After final pathological findings of surgical specimens, 2 additional partial resections and 1 total mastectomy were performed.

Conclusion: A second biopsy of US-MMT to the suspicious lesions around the main tumor could determine the optimal area of resection, contribute to reduce over- or under-surgery. We recommend the use of US-MMT to suspicious spreading lesions as a second biopsy as well as main lesions.

Poster Discussion

PO05-30

SCREENING MR EXAMINATIONS IN WOMEN WHO HAD UNDERGONE BREAST CONSERVING THERAPY FOR BREAST CANCERS

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Background/Purpose: To investigate whether the screening MRI can detect additional cancers in women who had undergone breast conserving therapy for breast cancers and screening mammography

Methods: Between January 2008 and December 2010, a total of 359 women (mean age, 46; range 25-64 years) who had undergone breast conserving therapy for breast cancers underwent screening MRI. The inclusion criteria were follow-up data of more than one year, no symptoms suggesting recurrence, and no current chemotherapy or distant metastasis. Mean follow up duration was 20.7 months (range, 13-47). The final assessment categories of mammography (n = 373) just prior to MRI were BI-RADS category 1 (n = 226), C2 (n = 118), and C3 (n = 29). Diagnoses of MRI-detected cancers were confirmed by means of MR-guided biopsies or correlative US-guided biopsies. Absence of breast cancer was determined by means of biopsy or the absence of positive findings on at 1 year follow-up imaging. Frequency of biopsy recommendations, positive predictive value (PPV), and tumor characteristics at MRI screening were evaluated.

Results: Of the 359 women, 26 biopsies were performed based on abnormal mammographic findings. Eight cancers (PPV3 = 30.8%) including 6 invasive ductal carcinomas (IDC) (mean size, 0.8cm; range, 0.4-1.4; all node negative) and 2 ductal carcinoma *in situ*, in 7 women (1.9%) were diagnosed. Two false negative cases (0.6%) were found; one IDC detected by PET/CT scan 5 months later and one axillary lymph node metastasis 6 months later.

Conclusion: In women who had undergone breast conserving therapy for breast cancers, MRI can detect minimal breast cancers that had not been identified on screening mammography.

PO05-31

THE NIPPLE ASPIRATE FLUID COLLECTION SUCCESS RATE WITH HALO SYSTEM IN BREAST CANCER PATIENTS IN KOREA

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Background/Purpose: Nipple aspirate fluid (NAF) cytology is a simple noninvasive method to study the ductal system of the breast. Especially in young patients who has dense breast, NAF used for early diagnosis of breast disease. But, till now it is rare, using NAF for diagnostic tool in Korea breast cancer patients. In the current study, we study who has high NAF collection success rate among breast cancer patients.

Methods: 50 patients with biopsy confirmed invasive carcinoma with or without a history of preoperative neoadjuvant chemotherapy in Asan medical center were included. Nipple aspirate fluid was collected by HALO NAF Collection System (NeoMatrix, Irvine, CA) before surgery. They had scheduled modified radical mastectomy

Results: : Nipple aspirate fluid was obtained from 50 women, including 14 who had received preoperative neoadjuvant chemotherapy. The median age of patients was 48 years. Eleven were obtain NAF either at least one. But only 7 specimens (14%) were inadequate fluid (> 1 mL), and 1 (2%) was malignant. Thirty-eight were checked the question compare with mammography in pain or discomfort, only 4 (15%) complain than mammography. Only one patient (2%) had complication that is nipple skin erosion. Patients treated with chemotherapy had not obtained. Young age group (OR 2.27), nullipara patient group (OR 1.75), without breast cancer family history group, without breast feeding experience group (OR 1.97), dense breast group (OR 1.45), obesity group (BMI > 25) (OR 4.667) were favorable NAF collection rate.

Conclusion: Young age group, nullipara, without breast feeding experience group, dense breast group, obesity group were favorable NAF collection rate.

PO06-01

RECONSTRUCTION WITH IMPLANT FOR MASTECTOMY PATIENTS OF BREAST CANCER

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Background/Purpose: Mastectomy for the operation of breast cancer has been performed for decades in women. Recently the issue for quality of life, and cosmetic satisfaction is increasing more and more, therefore many women have become interested in importance of breast reconstruction after their mastectomy.We would like to report about delayed reconstruction with cohesive gel implant for previously operated breast cancer patients.

Methods: September 2007 to May 2011, breast reconstruction with cohesive gel implant is performed in 24 patients. We identified all women who underwent delayed reconstruction with implant after mastectomy, on average 43.2 months after mastectomy. We have performed various reconstruction methods with implant (implant reconstruction only 15 patients/ with contra-lateral reduction 3/ with contra-lateral augmentation 4/ with mastopexy 2).

Results: The average satisfaction of patients after surgery was more than eight points (8 for 10).

Conclusion: To reduce the inconvenience caused in breast cancer patients after mastectomy, reconstruction with cohesive gel implant might be convenient and easy way for improving the quality of life and cosmetic satisfaction of patients.

PO06-02

A PATH ANALYSIS: A MODEL OF DEPRESSION IN KOREAN WOMEN WITH BREAST CANCER

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Background/Purpose: The purpose of this study was to test a hypothetical model of depression in Korean women with breast cancer and to test the mediating effects of self-esteem and hope.

Methods: Design: Cross-sectional design Setting: Participants were recruited from 3 general hospitals and 1 cancer hospital in the area of Busan, Korea Samples: 214 Korean women diagnosed with breast cancer (Stage I-III) Methods: All participants completed questionnaires (Zung's Self Rating Depression Scale, Herth's Hope Scale, Rosenberg's Self-Esteem Scale, Health Self Rating Scale, Kang's Family Support Scale). Based on the literature, the Mplus 3.0 program of the Muthen and Muthen company was used to determine the best depression model using path analysis

Results: Self-esteem was directly affected by perceived health status, religious beliefs, family support, economic status and fatigue. Hope was directly affected by how patients perceive their health status, family support and self-esteem. Depression was directly affected by self-esteem and hope. This path analysis model explained 31.3% of the variance in depression in Korean women with breast cancer.

Conclusion: A model of depression in Korean women with breast cancer was developed and the self esteem and hope affected on depression as mediating factors. The results have implications for nursing practice and research, specifically that self-esteem and hope must be considered in developing services to reduce depression in Korean women with breast cancer.

Poster Discussion

PO07-01

CARBONIC ANHYDRASE 9 IS A USEFUL SURROGATE MAKER TO PREDICT CHEMOSENSITIVITY AND PROGNOSIS OF NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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Background/Purpose: Current studies have demonstrated that neoadjuvant chemotherapy (NAC) improves survival outcomes and increases the chance for breast conservation when applied preoperatively. However, no reliable maker to predict chemosensitivity of NAC is available. Hypoxia regions exist in breast cancer tissues. A hypoxia condition increases metastasis and resistance to therapy of cancer cells, enhancing malignancy. Here, we focused on the significance of a hypoxia marker, carbonic anhydrase 9 (CA9), whose expression is induced by a hypoxia inducer, HIF-1. The aim of this study was to evaluate the value of CA9 as a surrogate maker of NAC for breast cancer.

Methods: A total of 102 patients with breast cancer of stage II and III, as evaluated by core needle biopsy and ultrasonography, was treated with NAC. Expressions of CA9, estrogen receptor, progesterone receptor, and HER2 were assessed by immunohistochemistry.

Results: The clinical complete response rate of all patients was 18% (18/102),partial response (PR) was 61% (62/102), no change was 20% (20/102),and progressive disease was 2% (2/102). The response rate (RR) was 78% (80/102).The pathological complete response rate (pCR) was 29%. The pCR rate of CA9-positive tumors was significantly lower than that of CA9-negative tumors. CA9 expression showed a poor disease free survival and overall survival time. A multivariate logistic regression analysis showed that the CA9 expression significantly correlated with disease free survival.

Conclusion: Hypoxia might be associated with aggressive tumor of breast cancer. Carbonic anhydrase 9 is a useful surrogate maker to predict chemosensitivity and prognosis of neoadjuvant chemotherapy for breast cancer.

PO07-02

THE RELATIONSHIPS OF LYMPH NODE RATIO TO RECURRENCE AND SURVIVAL ACCORDING TO MOLECULAR SUBTYPES OF BREAST CANCER

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[2]*Department of Pathology, Samsung Medical Center, Korea*
[3]*Department of Surgery, Konkuk Univ. Medical Center, Korea*

Background/Purpose: Previous studies suggest that nodal ratio (ratio of positive over excised lymph nodes) may have prognostic value in breast cancer. In this study, we evaluated cutoff values of the lymph node ratio (LNR) and compared the impact of LNR on disease-free survival (DFS) and overall survival (OS) in each molecular subtype of patients with that of N stage.

Methods: We reviewed the medical records and pathological slides of 666 breast cancer patients with metastatic axillary lymph nodes who underwent surgical treatment at the Samsung Medical Center in Korea, from January 1995 to December 2003. Molecular subtypes were defined by estrogen receptors (ER), progesterone receptors (PR) and HER2 expression status.

Results: Out of the 666 patients, 55.3% were luminal A type (ER+ and/or PR+, HER2-); 12.9% were luminal B type (ER+ and/or PR+, HER2+); 11.3% were HER2 type (ER-, PR-, HER2+); and 20.6% were triple-negative (TN) type (ER-, PR-, HER2-). The median follow-up duration was 8.1 years. Both DFS and OS rates were significantly worse in patients with LNR values greater than each cutoff value by subtype compared to patients with LNR values less than the cutoff values in luminal A, luminal B and TN. The significant LNR cutoff values for DFS and OS were 25.5% and 22.0% (luminal A), 9.5% and 18.5% (luminal B), 23.3% and 23.3% (TN).

Conclusion: LNR was a more significant factor for predicting of DFS and OS than N stage in each molecular subtype of breast cancer, except for the HER2 subtype.

PO07-03

SILVER-ENHANCED *IN SITU* HYBRIDIZATION AS AN ALTERNATIVE TO FLUORESCENCE *IN SITU* HYBRIDIZATION FOR ASSAYING HER2 AMPLIFICATION IN CLINICAL BREAST CANCER

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[2]*Department of General Surgery, Inje Univ. Sanggye Paik Hospital, Korea*

Background/Purpose: The goal of this study was to examine the feasibility of the newly developed silver-enhanced *in situ* hybridization technique as an alternative to fluorescence *in situ* hybridization for HER2 assay in primary invasive breast cancer.

Methods: Silver-enhanced *in situ* hybridization technique and fluorescence *in situ* hybridization for HER2 assay were used in 257 consecutive breast cancers.

Results: HER2 amplification was observed in 62 (23.1%) of 257 breast cancers based on silver-enhanced *in situ* hybridization. Of the 241 breast cancers measured using both methods, the results of the two methods were consistent in 231 (concordance: 95.8%; kappa = 0.903). When we compared HER2 amplification in the primary tumor with the metastatic lymph nodes of the same patients, HER2 amplification was observed in nine cases (10.3%) in which HER2 was not amplified in the primary tumors. In contrast, HER2 status was completely preserved in metastatic lymph nodes showing HER2 amplification in the primary tumor.

Conclusion: These results indicate that silver-enhanced *in situ* hybridization may be a viable alternative to fluorescence *in situ* hybridization in the clinical setting. In node-positive breast cancer, confirmation of the HER2 status of the metastatic lymph nodes appears to be mandatory, regardless of the HER2 status of the primary tumors.

PO07-04

THE CLINICAL SIGNIFICANCE OF P53 GENE SOMATIC MUTATION IN HER2 SUBTYPE KOREAN BREAST CANCER PATIENTS

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Background/Purpose: The coexistence of HER2 overexpression/amplification (HER2-positive) and p53 protein accumulation have been reported as strong prognostic factor in breast cancer. We investigated the clinical value of p53 mutation in HER2 subtype [hormone receptor (HR) negative and HER2-positive] Korean breast cancer patients by gene sequencing method.

Methods: We assembled clinicopathologic and molecular data on 485 cases who diagnosed, treated and analyzed for p53 mutation by the Immunohistochemical staining and the polymerase chain reaction-denaturing high performance liquid chromatography method for analyzing exon 5 to exon 9 in Gangnam Severance Breast Cancer Center, Seoul, Korea between December 2002 and December 2009. Median follow-up period was 51 months (1-100 months).

Results: Of 485 cases, 148 (30.5%) were HER2-positive, and 80 (16.5%) were HER2 subtype tumor, and 74 (15.3%) had p53 gene mutations, 36 (24.3%) in HER2-positive and 23 (28.8%) in HER2 subtype. In HER2-positive (regardless of HR status), there were no prognostic effect of p53 mutations by gene sequencing for disease-free survival (DFS) and overall survival (OS), $p = 0.714$, $p = 0.104$, and in HER2 subtype, $p = 0.290$, $p = 0.105$, respectively. When the patients with HER2 subtype were grouped by the presence or absence of p53 missense mutations, better DFS was noted in the absence p53 missense mutations group, and they were statistically significant ($p = 0.016$), however, not for OS ($p = 0.245$) neither with HER2-positive (DFS, $p = 0.100$; OS, $p = 0.243$).

Conclusion: Our study suggests that p53 missense mutation in HER2 subtype may be clinically relevant with DFS.

PO07-05

PROGNOSTIC INFLUENCE OF TUMOR LOCATION IN BREAST CANCER

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Background/Purpose: We investigated the prognostic influence of tumor location on the survival of breast cancer patients.

Methods: Data of 61,411 primary breast cancer patients from the Korean Breast Cancer Registry was analyzed. Tumor locations were classified into 6 groups; upper-outer quadrant, lower-outer quadrant, upper-inner quadrant, lower-inner quadrant (LIQ), central lesion, and overlapping lesion.

Results: LIQ, central lesion, and overlapping lesion showed lower survival rates than those of other 3 quadrants (log-rank test, $p = 0.031$, $p < 0.001$, and $p < 0.001$, respectively), and showed statistical significances in multivariate analyses (hazard ratio [HR], 1.326, 1.238, and 3.601; 95% confidence interval [CI], 1.040 to 1.691, 1.069 to 1.434, and 2.923 to 4.436; $p = 0.023$, $p = 0.004$, and $p < 0.001$, respectively). LIQ showed favorable clinicopathologic features as compared with other 3 quadrants, but central lesion and overlapping lesion showed poorer clinicopathologic features than the other tumor locations. However, although LIQ showed lower survival rates in the subgroups with no chemotherapy and/or no radiation therapy (log-rank test, $p = 0.002$, $p = 0.041$, respectively), there were no survival differences in the subgroups with chemotherapy and/or radiation therapy.

Conclusion: LIQ showed a lower survival rate, and internal mammary node was suggested to play a key role in this condition. Central lesion and overlapping lesion showed much lower survival rates than those of the other tumor locations. Consideration of tumor location as a prognostic factor in breast cancer could be helpful for appropriate staging, treatment, and prognostication in clinical setting.

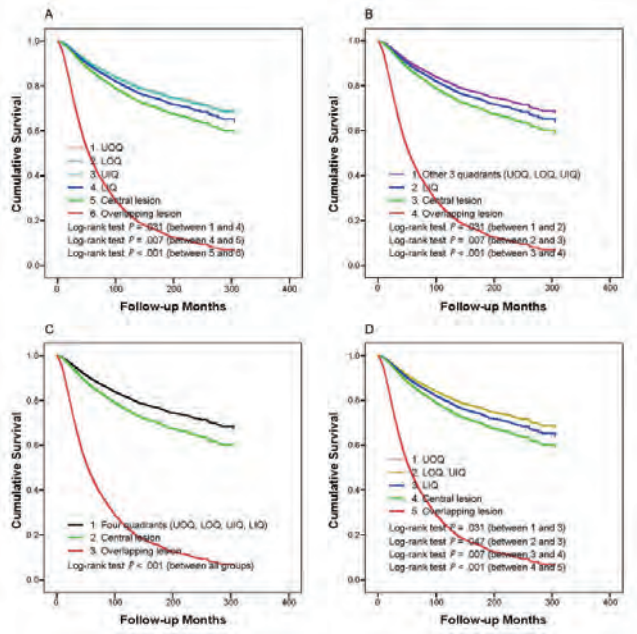
A
Cumulative Survival
1. UOQ
2. LOQ
3. UIQ
4. LIQ
5. Central lesion
6. Overlapping lesion
Log-rank test P = .031 (between 1 and 4)
Log-rank test P = .007 (between 4 and 5)
Log-rank test P < .001 (between 5 and 6)
Follow-up Months
B
Cumulative Survival
1. Other 3 quadrants (UOQ, LOQ, UIQ)
2. LIQ
3. Central lesion
4. Overlapping lesion
Log-rank test P = .031 (between 1 and 2)
Log-rank test P = .007 (between 2 and 3)
Log-rank test P < .001 (between 3 and 4)
Follow-up Months
C
Cumulative Survival
1. Four quadrants (UOQ, LOQ, UIQ, LIQ)
2. Central lesion
3. Overlapping lesion
Log-rank test P < .001 (between all groups)
Follow-up Months
D
Cumulative Survival
1. UOQ
2. LOQ, UIQ
3. LIQ
4. Central lesion
5. Overlapping lesion
Log-rank test P = .031 (between 1 and 5)
Log-rank test P = .047 (between 2 and 3)
Log-rank test P = .007 (between 3 and 4)
Log-rank test P < .001 (between 4 and 5)
Follow-up Months

Fig. 1

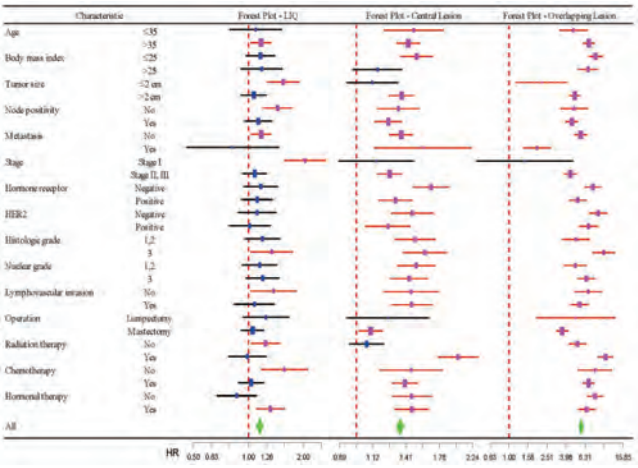
Characteristic
Forest Plot - LIQ
Forest Plot - Central Lesion
Forest Plot - Overlapping Lesion
Age
<35
>35
Body mass index
≤25
>25
Tumor size
≤2 cm
>2 cm
Node positivity
No
Yes
Metastasis
No
Yes
Stage
Stage I
Stage II, III
Hormone receptor
Negative
Positive
HER2
Negative
Positive
Histologic grade
1,2
3
Nuclear grade
1,2
3
Lymphovascular invasion
No
Yes
Operation
Lumpectomy
Mastectomy
Radiation therapy
No
Yes
Chemotherapy
No
Yes
Hormonal therapy
No
Yes
All
HR

Fig. 2

PO07-06

THE CLINICOPATHOLOGIC CHARACTERISTICS AND SURVIVAL OF THE ELDERLY BREAST CANCER PATIENTS

Hyewon Hwang, Jun Sang Lee, Si Mon Ko, Seho Park, Seung-il Kim, Byeong-woo Park

Department of General Surgery, College of Medicine, Yonsei Univ., Korea

Background/Purpose: Since 2000s, Korea has become an elderly society. But, there is no consensus on the optimal treatments for elderly breast cancer patients. This study aims to assess the characteristics and outcomes of elderly breast cancer patients (≥ 70: G1) compared to those of postmenopausal patients ($55 \leq$ age < 70: G2)

Methods: The clinicopathological characteristics & survival of 1547 breast cancer patients treated between 1986 and 2009 were retrospectively analyzed by Chi square tests, Kaplan-Meier method, Cox's Regression. We used the Charlson comorbidity index (CCI) to scoring the comorbidity.

Results: G1 was 188 (12.2%) and G2 was 1,359 (87.8%). There was no significant difference in tumor characteristics. G1 had higher CCI score than G2. G1 frequently performed total mastectomy and less frequently received radiotherapy and adjuvant chemotherapy. In G1, the death due to other cause was higher than G2. G2 had a better overall survival ($p < 0.001$) but, there was no significant difference in disease free survival. In G1, we analyzed the overall survival according to CCI. CCI 0 had best overall survival and over CCI 3 had poor overall survival ($p = 0.023$). In Cox's regression, lobular neoplasia involvement, CCI ≥ 2, tumor size > 2 cm, estrogen receptor positive were remained to be significant for overall survival of G1.

Conclusion: There was no significant difference in clinicopathologic characteristics between G1 and G2. But the treatment and outcomes were different in these groups. Therefore in decision of treatment of the elderly breast cancer, we consider that the performance status, comorbidity and life expectancy.

PO07-07

THE DIFFERENT PROGNOSTIC IMPACT OF CIRCULATING TUMOR CELL ACCORDING TO MOLECULAR SUBTYPES IN OPERABLE BREAST CANCER: LONG-TERM FOLLOW-UP

Sung Bae Hwang, Hye Yoon Lee, Hoon Yub Kim, Eun Sook Lee, Jeoung Won Bae

Division of Breast and Endocrine Surgery, Korea Univ. Anam Hospital, Korea

Background/Purpose: Circulating tumor cells (CTC) clearly correlate with worse prognosis in patients with metastatic breast cancer, but there are little data with long-term follow-up on the clinical implication of the CTC in operable breast cancer subtypes. We explored the relationships between previous clinical factors and CTC in operable breast cancer, and the prognostic impact of CTC according to molecular subtypes

Methods: We retrospectively evaluated 166 patients with operable breast cancer (stage I-IIIA) diagnosed at Korea University Anam hospital from April 1997 to May 2003. CTC was detected by CK-20 mRNA expression in peripheral blood sample that was sampled just prior to surgery under general anesthesia. Clinocopathological characteristics, metastasis free survival (MFS) and overall survival (OS) were analyzed according to CTC status in molecular subtypes.

Results: CK-20 mRNA positive CTC was detected in 37 (22.3%) of 166 patients and not correlated with any previous clinical factors in univariate analysis ($p > 0.05$). After a median follow-up of 100 months, the patients with CK-20 mRNA positive CTC in operable breast cancer had a worse prognosis on MFS and OS ($p < 0.05$). Among molecular breast cancer subtypes, the patients with CK-20 mRNA positive CTC had a worse prognosis on MFS and OS in triple negative type and HER-2/*neu* type of breast cancer ($p < 0.05$).

Conclusion: Our results suggest that CK-20 mRNA positive CTC is a useful prognostic indicator to understand tumor progression especially in triple negative and HER-2/*neu* type of operable breast cancer.

Poster Discussion

PO07-08

PATIENT SATISFACTION ANALYSIS FOR DECISION IMPACT OF THE 21-GENE RECURRENCE SCORE® (RS) ASSAY

Reika In[1], Chizuko Nakagawa[1], Hiroshi Yagata[1], Atsushi Yoshida[1], Hiroyuki Takei[2], Seigo Nakamura[3], Hideko Yamauchi[1]

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[2]*Division of Breast Surgery, Saitama Cancer Center, Japan*
[3]*Department of Breast Surgery, Showa Univ. School of Medicine, Japan*

Background/Purpose: The 21-gene Recurrence Score® (RS) has been reported to estimate the risk of recurrence and was validated in Japanese women (Toi et al., Cancer, 2010). St. Luke's International Hospital ,Tokyo, Japan directed a prospective study on the treatment impact of the RS for women with early-stage breast cancer (ESBC) with estrogen receptor (ER) positive disease. We assessed the impact of RS on patients who used it to decide their treatment.

Methods: We enrolled patients with ER positive ESBC, including pre- and post-menopausal women with lymph node (LN) negative disease and post-menopausal women with LN positive disease. All participating patients completed pre- and post-RS questionnaires on confidence in decision making. We adapted a published Decisional Conflict Scale (Annette O'Connor, 1993) to evaluate the impact of RS testing.

Results: In this cohort, one hundred twenty-six cases were included. Total conflict scale score were decreased after RS; average score 29.5 to 21.9 ($p < 0.01$). All subscores were also improved; uncertainty subscore 45.4 to 30.6 ($p < 0.01$), informed subscore 26.7 to 22.4 ($p = 0.01$), values clarity subscore 28.9 to 22.4 ($p < 0.01$), support subscore 23.0 to 18.4 ($p < 0.01$), effective decision subscore 24.8 to 17.7 ($p < 0.01$).

Conclusion: RS reduced decisional conflict regarding adjuvant treatment in Japanese patients with ER positive ERBC.

PO07-09

IPSILATERAL BREAST TUMOR RECURRENCE PREDICTION WITH WEB-BASED NORMOGRAM IN KOREAN WOMEN

Seung Pil Jung[1], Se Kyung Lee[1], Sangmin Kim[1], Min Young Koo[1], Min-young Choi[1], Soo Youn Bae[2], Dong Hui Cho[1], Jeonghui Lee[1], Jiyoung Kim[1], Seok Jin Nam[1], Jung-hyun Yang[2], Jeong Eon Lee[3]

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Background/Purpose: IBTR! Breast Cancer Model (IBTR!) version 2.0 is web-based tool which predict the ten years risk of local recurrence after breast conserving therapy. This tool integrates seven prognostic factors (patient age, margin status, lymphovascular invasion, tumor size, tumor grade, use of chemotherapy and hormonal therapy) for local recurrence with or without radiation therapy. To validate IBTR! 2.0 for Korean breast cancer patients, Samsung Medical Center database was used between 1994 and 2001.

Methods: The IBTR! version 2.0 nomogram was tested against 354 patients who underwent breast conserving surgery with radiation therapy from Samsung Medical Center between 1994 and 2001. The individual database which was entered into IBTR! version 2.0 generate predictive local recurrence rate. The mean predicted and observed 10-year estimates were compared for the entire cohort and for four groups predefined by nomogram-predicted risks as previous Massachusetts General Hospital (MGH) validation study : group 1: < 3%; group 2: 3-5%; group 3: 5-10%; and group 4: > 10%.

Results: IBTR! version 2.0 predicted an overall 10-year Ipsilateral breast tumor recurrence (IBTR) estimate of 5.7% (95% CI, 5.4 - 6.0), while the observed estimate was 5.7% (95% CI, 2.9-8.4; p = 0.98). The predicted and observed IBTR estimates were: group 1 (70 cases): 2.3% vs. 1.7%, p = 0.74; group 2 (124 cases): 3.9% vs. 2.0%, p = 0.17; group 3 (137 cases): 7.3% vs.10.0%, p = 0.25; and group 4 (23 cases): 11.7% vs. 9.3%, p = 0.7.
Conclusion: IBTR! 2.0 is acceptable nomogram for predicting 10 years local recurrence using Samsung medical Center database. This nomogram may assist patient coun-

seling and medical decision making.

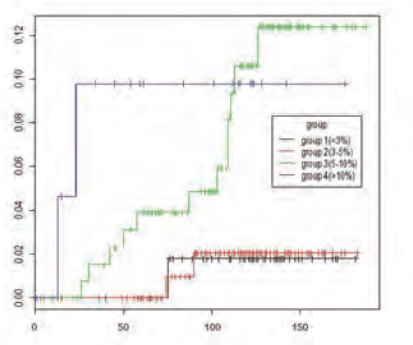

Fig. 1

Ten-Year Comparisons of Predicted and Observed IBTR Estimates										
			Predicted 10-Year IBTRI Version 2.0 Estimates(SE)			Observed 10-year IBTR Estimates(SE)			
Groups by predicted risk	No. of Patients	No. of IBTR Events	%	SE	95% CI Predicted	%	SE	95% CI Observed	P(t test)
I IBTR < 3%	70	1	2.3	0.05	2.2 to 2.4	1.7	1.77	0 to 5.2	0.75
II IBTR 3%-5%	124	2	3.9	0.05	3.8 to 4.1	2.0	1.42	0 to 4.8	0.17
III IBTR 5%-10%	137	12	7.3	0.14	7.0 to 7.6	10.0	2.92	4.3 to 15.7	0.25
IV IBTR > 10%	23	2	11.7	0.41	10.9 to 12.5	9.3	6.28	0 to 21.6	0.70
Overall	354	17	5.7	0.16	5.4 to 6.0	5.7	1.40	2.9 to 8.4	0.98

Table 1

PO07-10

CLINICOPATHOLOGIC AND PROGNOSTIC DIFFERENCE OF SCREEN DETECTED BREAST CANCER COMPARED WITH SYMPTOMATIC BREAST CANCER

Jiyoung Kim[1], Se Kyung Lee[1], Min Young Koo[1], Min-young Choi[1], Dong Hui Cho[1], Jeonghui Lee[1], Seung Pil Jung[1], Soo Youn Bae[2], Jeong Eon Lee[1], Jung-hyun Yang[1], Seok Jin Nam[1]

[1]*Department of Breast and Endocrine Surgery, Samsung Medical Center, Korea*
[2]*Department of General Surgery, Konkuk Univ. Medical Center, Korea*

Background/Purpose: Breast cancer screening program makes it possible to detect early cancer, thus to reduce breast cancer mortality. The authors studied clinicopathologic characteristics and prognosis of screen detected invasive breast cancer compared with symptomatic breast cancer. Furthermore, we compared the result according to molecular subtypes (luminal A, luminal B, Her2, triple negative), so intended to identify the role of screening in each subtypes.

Methods: From January 2002 to June 2008 , 3141 patients who underwent operation for the treatment of invasive ductal carcinoma (not otherwise specified) at Samsung medical center were included. Among them, 1,025 patient were screen detected, 2,116 patient were symptomatic, out of screening over 2 years. We reviewed the medical records retrospectively.

Results: Screening detected breast cancer was associated with smaller tumor size, more hormone receptor-positive, less lymph node involvement, lower stage and reduced mortality compared with symptomatic breast cancer ($p < 0.001$). According to the molecular subtype, in luminal A subtype, the result shows better pathologic feature and also better prognosis in screen detected cancer, significantly. And also screen detected breast cancer acts as an independent prognostic factor itself.

Conclusion: Compared to symptomatic breast cancer patients, screening detected breast cancer patients have favorable pathological and molecular characteristics, so better outcomes. According to the molecular subtype, only in luminal A subtype, screen detected breast cancer shows both overall and disease free survival benefit, and also acts as an independent prognostic factor itself. So, screening program seems to have a different efficacy depending on the molecular subtype of breast cancer

PO07-11

IMPACT OF TRIPLE NEGATIVE BREAST CANCER PHENOTYPE ON PROGNOSIS IN STAGE I BREAST CANCER

Jeong Eun Kim[1], Heui June Ahn[1], Jin-hee Ahn[1], Sung-bae Kim[1], Kyung-hae Jung[1], Dok Hyun Yoon[1], Gyung-yub Gong[2], Mi-jung Kim[2], Byung-ho Son[3], Sei-hyun Ahn[3], Seung Do Ahn[4]

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Background/Purpose: Although most stage I breast cancer have a good prognosis, they may have markedly different clinical outcomes. We assessed clinical outcome and prognostic factors of patients with stage I breast cancer by triple negativity.

Methods: Between January 1998 and December 2002, among 2,489 patients undergoing surgery, a total of 565 (23%) stage I breast cancer patients (tumor size 2 cm, and lymph node-negative) were reviewed retrospectively. Triple negative breast cancer (TNBC) was defined by a primary tumor that was estrogen and progesterone receptor negative (score < 3/8) and HER2 negative (HER2 0-2 and FISH- in case of HER2+).

Results: Out of 565 patients with stage I breast cancer, 90 patients (15.9%) were classified as TNBC. Proportion of patients with histologic grade 3 was higher in TNBC (48.9% vs. 34.3%, $p = 0.012$) and more patients with TNBC received adjuvant chemotherapy (78.9% vs. 56.2%, $p < 0.001$). Median follow-up time of 8.8 years, 74 recurrence occurred; 21(23.3%) in TNBC and 53 (11.2%) in non-TNBC ($p = 0.003$). At 3 years, incidence of recurrence was also higher in TNBC (16.7% vs. 8.0%, $p = 0.016$). In TNBC, 5 patients showed brain metastases, while 9 did in non-TNBC. Relapse-free survival (RFS) and survival rate were lower in TNBC (10-year RFS rate 75.1% vs. 87.6%, $p = 0.001$; 10-year survival rate 81.4% vs.91.3%, $p < 0.001$). On multivariate analysis, triple negativity and histologic grade were independent predictors of shorter RFS and survival.

Conclusion: TNBC had more aggressive clinicopathologic characteristics and poor survival in stage I breast carcinoma. More intensive adjuvant chemotherapy or different therapeutic strategy is warranted in this population.

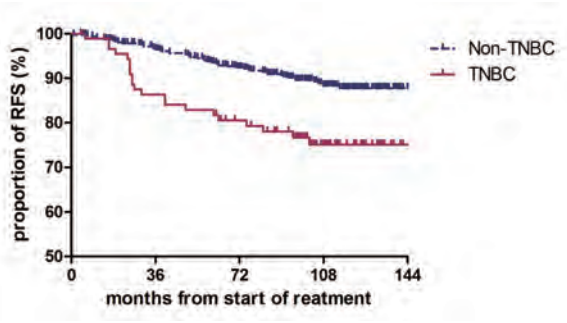
proportion of RFS (%)
100
90
80
70
60
50
0
36
72
108
144
months from start of reatment
Non-TNBC
TNBC

Fig. 1

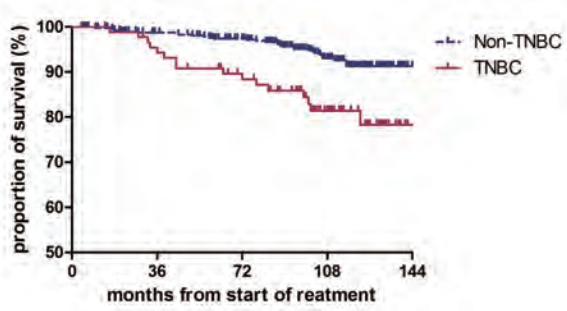
proportion of survival (%)
100
90
80
70
60
50
0
36
72
108
144
months from start of reatment
Non-TNBC
TNBC

Fig. 2

PO07-12

A RESPIRATORY CHALLENGE TO PREDICT THE OUTCOME OF BREAST CANCER TREATMENT

Jae Gwan Kim

School of Information & Communications/GMSE, Gwangju Institute of Science and Technology, Korea

Background/Purpose: Hyperoxic gases have been used to increase tumor oxygenation which in turn may improve the treatment efficacy since it has been known that hypoxic tumor cells are more resistant to radiation therapy, photodynamic therapy, and some types of chemotherapy. In this study, we tested whether tumor response to treatments can be predicted by monitoring tumor oxygenation during a hyperoxic gas intervention to animals.

Methods: We adapted two animal models which are Fisher 344 rats bearing mammary adenocarcinoma 13762NF and Brca1/p53 knockout mice model. Rat tumors (n = 9) were treated with a single dose of cyclophosphamide (100 mg/kg, i.p.) and mice tumors (n = 8) were treated with cisplatin (1.2 mg/kg, daily for a week). A respiratory challenge from air to 100% oxygen was given to animals before and post chemotherapy and tumor oxygenation levels were monitored by diffuse optical spectroscopy/imaging system.

Results: From the rat study, we found that the amplitude and rate of tumor oxygenation change during a hyperoxic gas intervention are getting smaller and becoming slower as tumors show responses to the treatment. We also found from the mice tumor study that the amplitude of tumor oxygenation change during a respiratory challenge even before the chemotherapy starts can potentially predict whether the tumor will respond to the treatment or not.

Conclusion: Our preliminary results show that a combination between a simple respiratory intervention to tumor and a tumor oxygenation monitoring tool such as diffuse optical spectroscopy/imaging may play an important role in early prediction of cancer treatment and can be easily translated to clinical test.

PO07-13

KI-67 AS PREDICTORS OF RESPONSE IN LOCALLY ADVANCED BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Background/Purpose: Neoadjuvant chemotherapy is well established in the treatment of large potentially operable and locally advanced breast cancer. The objective of this study was to compare the prognostic significance of proliferation, as assessed by Ki-67 expression, before neoadjuvant chemotherapy for women with advanced breast carcinoma.

Methods: Fifty-six patients who underwent neoadjuvant chemotherapy between 2005 and 2010 were included for this study. The expression of Ki-67 was assessed using immunohistochemistry in pre-therapy core-needle biopsy and post-therapy surgical excision specimens. The following factors were considered pre- and post-chemotherapy for their relationship with relapse-free. Statistical analyses were performed with Mann Whitney U test, Multiple logistic regression, and Kaplan-Meier method and using SPSS 12.0.

Results: Clinical response was rated as complete response (CR) for 5 patients (8.9%), partial response (PR) for 26 patients (46.5%), Stable disease (SD) for 25 patients (44.6%), and progressive disease (PD) for 0 patients. The mean Ki-67 value of tumors with CR was 50.0%, the Ki-67 value of tumors with PR was 39.6%, and the Ki-67 value of tumors with SD was 21.9%. There was a significant difference between them ($p = 0.02$). The disease-free survival rate of patients between lower Ki-67 values ($< 25\%$) and higher values ($> 25\%$) was not significantly different ($p = 0.19$).

Conclusion: The results of our study suggest that the Ki-67 value before neoadjuvant chemotherapy is a predictive factor for the effectiveness of neoadjuvant chemotherapy. A higher Ki-67 reveals a higher PR rate. An individualized treatment plan is important for patients with breast cancer now and will be more so in the near future.

PO07-14

KI67 AND P53 AS PROGNOSTIC FACTORS FOR LUMINAL TYPE BREAST CANCER

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Background/Purpose: Breast cancer encompasses a heterogeneous population of tumors characterized by a variety of clinical, pathological, and molecular features. The estrogen receptor (ER) or progesterone receptor (PR) positive luminal type in breast cancer was known of better prognosis but less chemosensitivity. The aim of the study was to investigate the outcomes and the prognostic factors for the ER (+) or PR (+) luminal subtype in patients with breast cancer.

Methods: In an investigation of 405 women with breast cancer who underwent surgery from 1994 and 2000, the expressions of ER and PR, and human epithelial receptor-2 (HER2) were evaluated. Medical records were retrospectively reviewed to find clinicopathological features.

Results: To study subgroup analysis, the hazard ratio of the luminal A and B subtypes were 1.63 (95% CI, 0.46-5.73; $p = 0.45$) and 2.43 (95% CI, 1.44-4.09; $p < 0.01$), respectively. A univariate analysis showed that the pathological tumor stage, the pathological axillary lymph node status were prognostic factors of recurrence free survival (RFS) and overall survival (OS). However, the ki67 expression and the p53 expression were associated with OS only in the univariate analysis.

Conclusion: The Ki67 expression related to important prognostic factor in terms of both the RFS and the OS in patients with breast cancer by luminal type. In addition to, in study subgroup analysis, the Ki67 as well as p53 were reliable to important prognostic factor in aspect of OS. Therefore, the more intensive adjuvant treatment will improve the OS in patients by luminal A subtype with ki67 or p53 expression.

PO07-15

ABCB1 SINGLE NUCLEOTIDE POLYMORPHISMAS A POSSIBLE PROGNOSTIC FACTOR IN BREAST CANCER PATIENTS RECEIVING DOCETAXEL AND DOXORUBICIN NEOADJUVANT CHEMOTHERAPY ON SYSTEMIC TREATMENT

Hee Jun Kim[1], Kyung-hun Lee[1], Seock-ah Im[2], In Jin Jang[3], So Jeong Yi[3], Bhumsuk Keam[1], Yu Jung Kim[4], Sae-won Han[2], Do-youn Oh[2], Jee Hyun Kim[5], Nariya Cho[6], Eui Kyu Chie[7], Wonshik Han[8], Woo Kyung Moon[9], Tae-you Kim[2], Dong-young Noh[8], In Ae Park[10], Yung-jue Bang[2], Sung Whan Ha[11]

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[8]*Department of General Surgery, Seoul National Univ. Hospital, Korea*
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Background/Purpose: Expression of the adenosine triphosphate-binding cassette B1 (ABCB1) transporter and P-glycoprotein are associated with resistance to chemotherapy. The purpose of this thesis was to investigate the role of single nucleotide polymorphism in the ABCB1 and CYP3A genes in breast cancer patients treated with neoadjuvant chemotherapy.

Methods: Patients with histologically confirmed breast cancer, Stage II or III, referred for neoadjuvant chemotherapy were enrolled. Patients were treated with 3 cycles of neoadjuvant and adjuvant chemotherapy with docetaxel and doxorubicin. The polymorphisms of ABCB1 (C3435T, G2677T/A, and C1236T) and CYP3A were genotyped. The correlation of genetic polymorphisms of ABCB1, CYP3A, and clinical outcomes was analyzed.

Results: Between September 2003 and September 2008, 216 patients were enrolled. ABCB1 3435TT genotype had a longer overall survival (OS) than CT/TT. Multivariate analyses for the OS revealed that Performance Status (PS), initial clinical stage, and triple negative phenotype were significantly associated with the OS. ABCB1 3435TT genotype was also associated with a lower risk of death with marginal significance ($p = 0.071$). ABCB1 3435TT genotype had a higher AUC than CC/CT genotype for docetaxel ($p = 0.031$). These higher AUCs in the C3435TT genotype was associated with increased toxicities of neutropenia ($p = 0.037$) and diarrhea ($p = 0.017$).

Conclusion: This study showed that the genetic polymorphism of ABCB1 C3435T might be associated with a longer OS. Our results also suggest that the prediction of docetaxel toxicity might be possible for ABCB1 C3435T polymorphism. Larger prospective studies as well as functional studies in human subjects are warranted.

PO07-16

PREDICTION OF RESPONSE TO DOCETAXEL USING MRNA EXPRESSION AND CPG METHYLATION PROFILES IN TRIPLE-NEGATIVE BREAST CANCER CELL LINES

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[1]*Department of Surgery, Korea Institute of Radiological & Medical Sciences, Korea Cancer Center Hospital, Korea*
[2]*Department of Surgery, Seoul National Univ. Hospital, Korea*
[3]*Department of Biochemistry, College of Medicine, Seoul National Univ., Korea*
[4]*Department of Surgery, Dongnam Institute of Radiological & Medical Sciences, Korea*
[5]*Cancer Research Institute, College of Medicine, Seoul National Univ., Korea*

Background/Purpose: Neoadjuvant chemotherapy studies have consistently reported higher response rates in triple-negative breast cancer (TNBC) than non-TNBC, and pathologic complete response has been shown to predict improved long term outcomes for TNBC. In this study, we investigated the genetic and epigenetic alterations associated with chemo-responsiveness in TNBC.

Methods: Using a panel of nine TNBC cell lines and docetaxel, the differentially expressed genes (DEGs) associated with docetaxel responsiveness were assessed. CpG methylation statuses were analyzed to evaluate the significance of epigenetic regulation of genes in docetaxel responsiveness of TNBC. In addition, by analyzing three public datasets, we evaluated whether the DEGs associated with docetaxel responsiveness from an *in vitro* study can predict clinical outcomes of patients with TNBC.

Results: Up-regulated DEGs with increasing docetaxel resistance included many genes involved in inflammatory response, and many canonical pathways related to inflammatory response were significantly enriched in the up-regulated DEGs. Combined analysis of gene expression and CpG methylation showed that several DEGs involved in inflammatory response were up-regulated by CpG hypomethylation with increasing docetaxel resistance and DEGs down-regulated by CpG hypermethylation included several genes related with apoptosis, immune response, or programmed cell death. In the analysis of public datasets, several DEGs related with docetaxel responsiveness in a cell line study were found to be associated with clinical outcomes.

Poster Discussion

Conclusion: Our results suggest high expression of genes associated with inflammatory response may play a key role in docetaxel resistance of TNBC. The DEGs associated with chemo-responsiveness from an *in vitro* study can predict clinical outcomes of patients with TNBC.

PO07-17

WEIGHT CHANGES AFTER BREAST CANCER THERAPY IN KOREA

Soo Hyun Kim

Department of Nursing, Inha Univ., Korea

Background/Purpose: The purpose of this study was to examine weight changes, factors associated with weight gain in regard to socio-demographic aspects, clinical aspects, and health behavior characteristics, and relationships between weight gain and emotional distress in breast cancer survivors after cancer therapy.

Methods: A total of 132 disease-free breast cancer survivors (mean age, 50.3 years; mean time since diagnosis, 34.3 months) were recruited from a comprehensive hospital in Korea. Subjects completed a self-reported measurement, which included the Hospital Anxiety and Depression Scale and Mini Dietary Assessment, and height and weight were measured.

Results: Mean ± SD weight changes were -0.08 ± 4.28 kg (range = -14.40-12.90). Twenty-one percent of the sample gained more than 5% weight at diagnosis, 58.3% maintained weight, and 21% lost weight. Factors associated with weight gain were having a job, obesity at diagnosis, longer time since diagnosis, sedentary lifestyle, and poor diet quality. In multivariate logistic regression analysis, more than 36 months since diagnosis (OR = 9.29; p = 0.001), poor diet quality (OR = 6.57; p = 0.006), and obesity at diagnosis (OR = 4.41; p = 0.019) were associated with increased risk weight gain after breast cancer therapy. Women who gained weight reported higher levels of anxiety and depression than women who did not gain weight; however, those were not statistically significant.

Conclusion: In long-term survivors, Korea women having poor diet quality and obesity at diagnosis should be considered to be at high-risk for weight gain after breast cancer therapy.

PO07-18

THE PROGNOSTIC SIGNIFICANCE OF METAPLASTIC CARCINOMA OF BREAST: A COLLECTIVE COMPARISON STUDY WITH OTHER COMMON BREAST CANCERS

Hung-Wen Lai, Ling-ming Tseng, Tsai-wang Chang, Sou-jen Kuo, Shou-tung Chen, Dar-ren Chen

Department of General Surgery, Chunghua Christian Hospital, Taiwan

Background/Purpose: Metaplastic carcinoma of the breast (MCB) is a rare histological subtype of breast cancer with incidence less than 1%. Due to its rarity, the clinical characteristics and prognostic significance of MCB compared with other common breast cancer like invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC) are unclear and controversial between different reports.

Methods: Cases of MCB were enrolled from 4 medical centers in Taiwan. The patients' demographic data, tumor characteristics and prognosis of MCB were analyzed and compared with IDC, and ILC. To further clarify the prognostic difference between MCB and IDC, a case control analysis was performed to minimize the effect of tumor size, lymph node status and other clinicopathologic factors. The disease free survival (DSF) and overall survival (OS) between groups were compared.

Results: Forty-five MCB patients combined with 1777 IDC and 53 ILC patients from cancer registry database of Chunghua Christian Hospital (CCH) comprised the current study. Compared with IDC, MCB is associated with older age, larger tumor size, lesser lymph node positive rate, higher distant metastasis, higher tumor grade, lower estrogen receptor positive tumor, and higher triple negative breast cancer subtype. Compared with IDC, MCB was associated with worse OS ($p = 0.031$), but no difference in DSF ($p = 0.071$). While MCB was not statistically different from ILC in both DSF and OS ($p = 0.132$ and $p = 0.289$, respectively). Compared with cases controlled IDC group, the MCB patients remained showed poorer OS ($p = 0.040$), but not different in DSF ($p = 0.439$).

Conclusion: MCB is associated with poorer OS compared with IDC, and this poorer prognosis was related to tumor behavior rather than clinicopathologic factors.

Fig. 1 Comparison of MCB with IDC and ILC in DFS and OS

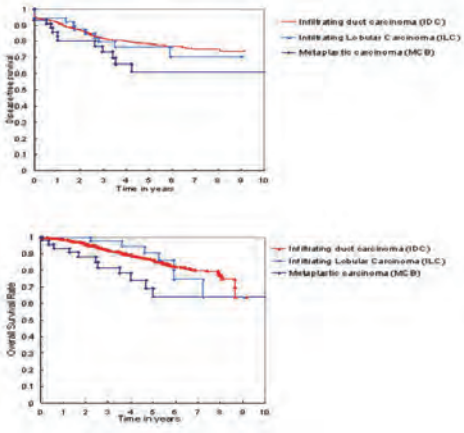

Fig. 1

Fig. 2 Comparison of MCB with cases controlled IDC in DFS and OS

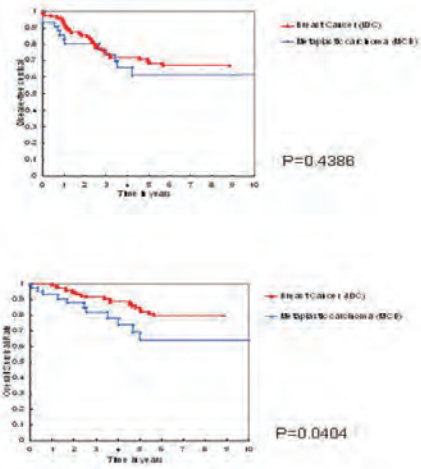

Fig. 2

PO07-19

THE CLINICAL SIGNIFICANCE OF ISOLATED TUMOR CELL AND MICROMETASTASIS OF SENTINEL LYMPH NODE IN KOREAN BREAST CANCER PATIENTS

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Background/Purpose: The clinical significance of isolated tumor cell (ITC) micrometastasis (MM) of sentinel lymph node (SLN) is controversial. The aim of this study is to investigate whether ITC or MM of SLN in Korean breast cancer patients influence on prognosis.

Methods: We had analyzed retrospectively 680 invasive breast cancer patients who treated with SLNB in Gangnam Severance Hospital between January 1995 and December 2007. Median follow-up period was 60 months (1-169 months). Probabilities for overall survival (OS) and disease-free survival (DFS) were estimated by Kaplan-Meier methods, and survival curves for different subgroups were compared by log-rank test. All reported p values are from two-sided tests.

Results: Of 680 patients, locoregional and/or systemic recurrence occurred in 46 patients (6.8%); 25 (6.7%) of 464 SLN negative, 2 (8%) of 25 ITC, 3 (10%) of 30 MM and 16 (9.9%) of 161 macrometastasis. Of 46 recurrences, 17 patients (37.0%) had died; 11 (2.4%) in SLN negative, 1 (4%) in ITC, none in MM and 5 (3.1%) in macrometastasis. In patients with ITC of SLN, axillary lymph node dissection and radiotherapy did not influence on DFS ($p = 0.957$, $p = 0.350$) and OS ($p = 0.355$, $p = 0.655$), respectively, neither in patients with MM, DFS ($p = 0.807$, $p = 0.938$).

Conclusion: We tentatively suggest that ITC and MM of SLN have no influence on clinical outcome in Korean breast cancer patients.

PO07-20

CLINICAL SIGNIFICANCE OF SERUM TUMOR MARKERS (CA15-3 AND CEA) IN SYSTEMIC RECURRED BREAST CANCER PATIENTS

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Background/Purpose: The purpose of this study was to evaluate the significance of serum tumor marker levels [cancer antigen 15-3 (CA15-3) and carcinoembryonic antigen (CEA)] at the time of systemic recurrence in breast cancer patients.

Methods: CA15-3 and CEA at the time of both diagnosis and recurrence were measured in 166 systemic recurred breast cancer patients with stage I-III between 1999 and 2009. The correlation between tumor marker levels at recurrence and clinicopahtological parameters with outcomes were investigated by chi-square test, univariate and multivariate analyses .

Results: Eighty-five patients (51%) had elevated CA15-3 levels at the time of recurrence and 58 patients (36%) had also elevated CEA levels at the time of recurrence. More advanced stage, elevated preoperative levels of CA15-3, bone metastasis, multiple metastases were significantly correlated with elevated CA15-3 levels at recurrence. On the other hand, elevated CEA levels at recurrence were significantly correlated with liver metastasis, elevated preoperative CEA levels. Patients with elevated serum tumor markers at the time of diagnosis and recurrence showed poor survival outcomes after recurrence than those with both normal group.

Conclusion: Our study suggests that elevated serum tumor markers in breast cancer patients at the time of recurrence are associated with preoperative tumor markers, specific site of recurrence, and metastatic burden. Therefore measurement of tumor markers could be useful in systemic recurred breast cancer patients.

PO07-21

HORMONE RECEPTORS EXPRESSION IN PHYLLODES TUMORS OF THE BREAST

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Background/Purpose: Phyllodes tumors (PTs) of the breast are fibroepithelial lesions showing proliferation of both epithelial and stromal components. Although the expression of hormonal receptors in mammary carcinoma is well documented, the data of hormonal receptors status in mammary PTs are relatively scant and inconsistent. The objective of this study was to ascertain the hormonal receptor profiles of the epithelial and stromal components of PTs and to determine their relationship with stromal proliferation.

Methods: Eighty two PTs (50 benign, 22 borderline, and 10 malignant) were studied. Automated immunohistochemical staining for estrogen receptor (ER)-α and β, progesterone receptor (PR), androgen receptor (AR), and Ki-67 was performed using tissue microarray blocks and assessed in both the stromal and epithelial components.

Results: The epithelial component demonstrated expression for ER-α (45.6%, 36/79), ER-β (37.2%, 29/78), PR (91.1%, 72/79) and AR (10.1%, 8/79). The stromal component was only positive for ER-β (26.8%, 22/82). The expression of ER-β was found to be correlated significantly with the expression of AR ($r = 0.352$, $p = 0.002$). No association between hormonal receptor expression and tumor grade of PTs was found. Stromal Ki-67 expression was statistically correlated with epithelial ER-β, epithelial AR, and stromal ER-β expression.

Conclusion: In conclusion, ER-β and epithelial AR expression in PTs was correlated with the proliferative rate in the stromal component. Immunohistochemical examination of ER-β and AR may have some impact on the postoperative management of the patients with PTs.

PO07-22

CLINICOPATHOLOGIC ASSESSMENTS AND POSTOPERATIVE OUTCOMES OF PATIENTS WITH POSITIVE SURGICAL MARGINS WHO UNDERWENT BREAST-CONSERVING SURGERY FOR PRIMARY BREAST CANCER

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Background/Purpose: Determination of clinicopathologic factors predicting involved surgical margins after breast-conserving surgery (BCS) is crucial for reducing local recurrence in patients with breast cancer.

Methods: Of 144 patients with primary breast cancer who underwent BCS between June 2005 and May 2010, forty-two patients with positive surgical margins (29.1%) were investigated. To determine factors responsible for positive surgical margins, tumor size, nodal status, tumor grade, hormonal and HER status, and findings in preoperative imaging tests were assessed.

Results: Involved surgical margins were due to intraductal spreading of carcinoma (ISC) in 69% and due to direct invasion of cancer in 31% of the patients. Tumor size, nodal status, and hormonal and HER2 status showed no relationship with the results. Preoperative imaging tests including mammography, echography and MRI demonstrated tumor appearance in 85.6% of the patients and findings indicating ISC only in 33% of the patients. Of these patients, thirty-three (79%) received boost radiotherapy (10 Gy) to the tumor bed after whole breast irradiation of 50 Gy, 4 (9.5%) received mastectomy and 5 (12%) received no intervention except for endocrine therapy. The patients were followed up for 13 to 72 months (mean period of 37 M). No local recurrence was observed.

Conclusion: In conclusion, it is possible to reduce the frequency of positive surgical margins after BCS by one third if we pay more attention to ISC on preoperative scanning modalities. However, novel modalities should be developed to detect more precisely the extension of cancer involvement.

PO07-23

THE IMPLICATION OF HORMONE RECEPTORS STATUS ON SURVIVAL IN LUMINAL A SUBTYPE BREAST CANCER PATIENTS RECEIVED ENDOCRINE THERAPY: THE NATIONWIDE KOREAN BREAST CANCER SOCIETY REGISTRATION PROGRAM

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Background/Purpose: The aim of study was to evaluate characteristics and outcomes according to estrogen receptors (ER) and progesterone receptors (PR) status in Korean luminal A subtype breast cancer patients received endocrine therapy between January 1996 and November 2006.

Methods: Using the Severance Hospital Registry of 1,180 luminal A subtypes and the nationwide Korean Breast Cancer Society (KBCS) database of 9,916 patients, clinicopathological features and survival were analyzed by a chi-square test, Kaplan-Meier methods, and Cox's models. Luminal A subtype was categorized into three subgroups as follows: ER(+)/PR(+), ER(+)/PR(-), and ER(-)/PR(+). All patients had HER2-negative tumor.

Results: ER(+)/PR(+), ER(+)/PR(-), and ER(-)/PR(+) subgroup constituted 74.6%, 20.1%, and 5.3% of the Severance Registry, respectively, and 73.4%, 17.2%, and 9.4% of the KBCS database, respectively. ER(+)/PR(+) subgroup showed trends toward smaller size and well-differentiation, ER(+)/PR(-) was the oldest age at diagnosis, and ER(-)/PR(+) was associated with the youngest age at diagnosis and grade III tumor based on the Severance Registry. These associations were confirmed by the KBCS database. Single hormone receptor-positive subgroups demonstrated poorer disease-related outcomes according to the Severance Registry. Similarly, by the KBCS database, ER(+)/PR(-) [relative risk (RR), 1.436; 95% CI, 1.137-1.814] and ER(-)/PR(+) (RR, 1.521; 95% CI, 1.123-2.062) subgroups showed a significantly higher risk for overall survival in multivariate analysis.

Conclusion: Our study suggests that luminal A subtype presents heterogeneous features and different endocrine-responsiveness according to hormone receptors status. Detailed classification and personalized management should be considered in patients with luminal A subtype breast cancer.

PO07-24

COMPARISON OF PROGNOSTIC FACTORS BETWEEN THE EARLY AND LATE RECURRENCE IN PATIENTS WITH METASTATIC BREAST CANCER

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Background/Purpose: Patients with recurrent breast cancer usually die of their disease, even after radical surgery and adjuvant therapies that reduce the odds of dying. Many studies are based on analyses comparing patients who died of recurrence with patients without recurrence. However, less attention has been paid to evaluating factors associated with the timing of recurrence. Thus, The objective of this study is to compare the recurrent patients within 2 years after operation and adjuvant therapies as the early recurrence with the those over 2 years as the late recurrence.

Methods: We retrospectively reviewed the data of 95 recurrent breast cancer patients who underwent curative surgery to determine the prognostic factors such as menopausal status, operation method, T state, N statge, histologic grade, nuclear grade, extensive intraductal component, hormone receptor, p53, c-erbB2 and Ki67. Correlation between various factors and the timing of recurrence was analyzed in two groups.

Results: Histologic grade ($p = 0.016$), nuclear grade ($p < 0.001$), p53 ($p = 0.022$) and Ki67 ($p < 0.001$) were significant different factors that influenced the systemic recurrence between early recurrence and late recurrence. In axillary lymph node negative breast cancer, histologic grade ($p = 0.031$), nuclear grade ($p = 0.007$) and Ki67 ($p = 0.001$) were significant factors that influenced the systemic early recurrence. In axillary lymph node positive breast cancer, nuclear grade ($p = 0.002$) and Ki67 ($p = 0.005$) were significant factors that influenced the systemic early recurrence.

Conclusion: Attention has been paid to evaluating factors such as Histologic grade, nuclear grade, p53 and Ki67 associated with the timing of recurrence. We suggest that these patients should be aggressive treated and be closely followed up.

PO07-25

TOPOISOMERASE II ALPHA EXPRESSION AND THE KI-67 LABELING INDEX CORRELATE WITH PROGNOSTIC FACTORS IN ER-POSITIVE AND HER2-NEGATIVE BREAST CANCER

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[1]*Department of Thoracic and Visceral Organ Surgery, Graduate School of Medicine, Gunma Univ., Japan*
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Background/Purpose: Topoisomerase II alpha (Topo IIa) plays a role in DNA replication and is a molecular target for anthracycline-based chemotherapy. The Ki-67 labeling index (LI) is an evaluation of tumor cell proliferation. The aim of this study was to evaluate relationships among Topo IIa expression, the Ki-67 LI, and prognostic factors in estrogen receptor (ER)-positive, human epidermal growth factor type-2 (HER2)-negative breast cancer.

Methods: Seventy-one patients were diagnosed with ER-positive, HER2-negative breast cancer between July 2003 and December 2004. Formalin-fixed, paraffin-embedded tumor specimens were stained for Topo IIa expression and Ki-67 LI. The level of Topo IIa expression and the Ki-67 LI were compared with clinical factors such as age, tumor size, progesterone receptor status, nodal status, nuclear grade, and lymphovascular invasion (LVI).

Results: A statistically significant difference was observed between Topo IIa overexpression, nuclear grade ($p = 0.036$), and LVI ($p = 0.029$). Topo IIa overexpression was statistically correlated with the Ki-67 LI ($p < 0.0001$). A statistically significant difference was observed between the Ki-67 LI and nuclear grade ($p = 0.01$). Survival analysis revealed the significant prognostic value of Ki-67 LI in patients with ER-positive, HER2-negative breast cancer ($p = 0.003$).

Conclusion: Ki-67 LI is a strong prognostic factor in ER-positive HER2-negative breast cancer. Topo IIa overexpression was significantly correlated with the Ki-67 LI, nuclear grade, and LVI. These findings suggest a role for Topo IIa expression as a proliferation marker and a prognostic factor in ER-positive, HER2-negative breast cancer.

Poster Discussion

PO07-26

THE COMBINATION OF P53, P21 AND MDM2 IMMUNOHISTOCHEMISTRY IS A PROGNOSTIC MARKER IN BREAST CANCER, EVEN IN ER+ AND HER2- SUBTYPE

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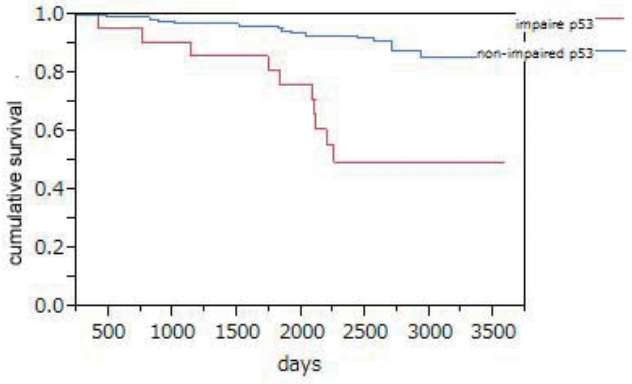
[2]*Ishinomaki Red Cross Hospital, Japan*

Background/Purpose: It is controversial whether p53 immunohistochemistry (IHC) serves as a prognostic marker for breast cancer, whereas p53 mutation has been confirmed as a marker by meta-analysis. The problems of p53 IHC include false negative (deletion mutant etc) and false positive (stabilization of wild type p53). p53 function is also disrupted by other proteins, such as MDM2. Recently, combinations of gene expression are shown to reflect tumor characters such as intrinsic subtype or Oncotype DX®. p21 is one of the major p53-regulated protein which controls cell cycle arrest. MDM2 is also a p53-targeted gene degrading p53. This study is initiated to improve accuracy of prognostic markers, with combination of p53 and p53-regulated protein.

Methods: IHC of p53, p21 and MDM2 were investigated in operated 157 breast cancers. Expressions of p53+ and/or MDM2+ and p21 were defined as impaired p53 and the others as non-impaired p53. The survival rates were evaluated by Kaplan-Meier method and log-rank test.

Results: Impaired p53 was 24 (15.3%). Five-year survival was 81.4% in impaired p53, 95.4% in non-impaired p53 (Fig. 1, $p < 0.0001$). Estrogen receptor (ER)+ and HER2- was 104 (66.2%). which included 11 (10.6%) impaired p53. In this subtype, 5-year survival was 81.8% in impaired p53, 96.7% in non-impaired p53 (Fig. 2, $p = 0.0012$).

Conclusion: The combination of p53, p21 and MDM2 IHC is useful prognostic marker and may help determine more aggressive treatment for breast cancer, especially in ER+ and HER2- subtype.


impaire p53
non-impaired p53
cumulative survival
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2500
3000
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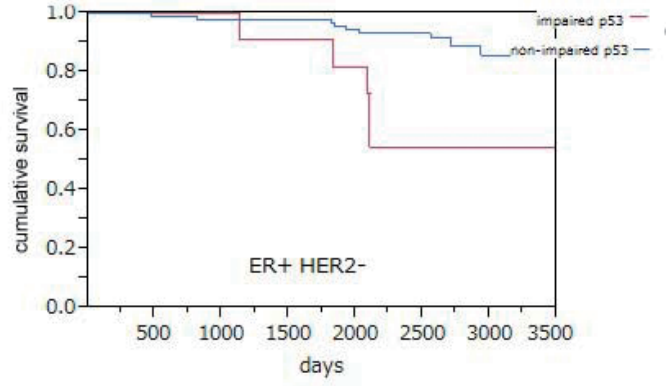
days

Fig. 1


impaired p53
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3500
days

Fig. 2

PO07-27

ROLE OF THE ADHESION MOLECULES CD49D AS A PROGNOSTIC MARKER OF INVASIVE BREAST CANCER

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Background/Purpose: CD49d is an integrin alpha subunit and it plays some role on cell to cell adhesion. The aims of this study are to determine the CD49d expression in primary breast cancer and evaluate the corresponding influence of CD49d on the clinical outcomes.

Methods: From 1995 to 2007, total 496 patients with stage I-III invasive breast cancer were included in this study. We examined the correlations between the CD49d expression and the breast cancer-related pathobiologic markers by performing immunohistochemistry. We analyzed CD49d expressions with respect to overall survival and relapse-free survival (RFS).

Results: All cases occurred in women with mean age of 47.33 ± 10.01 years old (range 25-81). Positive immunoreactivity for CD49d was noted in 20.2% of the patients. The expression of CD49d was correlated with triple negative subtype ($p = 0.050$) and low nuclear grade ($p = 0.045$). Median follow-up was 58.4 ± 29.6 months (range 12.7-160.3). In univariate analysis, nodal status ($p = 0.008$) and CD49d expression ($p = 0.000$) were significantly associated with relapse-free survival (RFS). Multivariate survival analysis showed that CD49d expression was an independent prognostic marker for RFS (hazard ratio, 0.308; 95% CI, 0.153-0.619; $p = 0.001$). In the group with adjuvant chemotherapy, CD49d positive patients had longer survival than CD49d negative patients ($p < 0.001$).

Conclusion: CD49d overexpression is significantly associated with low nuclear grade and an indicator of favorable RFS for patients with invasive breast cancer.

PO07-28

RELATIONSHIP BETWEEN TUMOR SIZE, LYMPH NODE INVOLVEMENT AND PROGNOSIS IN A LARGE COHORT OF PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER IN KOREA

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Background/Purpose: Patients with triple-negative breast cancer (TNBC) have shown that tumor size and lymph node status may not be linearly correlated with survival outcome, raising the doubt for the accuracy and independence of tumor size and number of positive lymph nodes in the prediction of clinical outcomes.

Methods: We reviewed 5,861 patients with TNBC diagnosed between 1999 and 2006 in Korean Breast Cancer Society Registry data. Patients were stratified by tumor size and lymph node status. The association of tumor size and lymph node status with overall survival (OS) was analyzed using Kaplan-Meier product limit method.

Results: Median age was 47 years (range, 21-89) and median follow-up was 37 months (range, 0-133). 745 (12.7%) of 5,861 patients with TNBC were dead. The 5-year OS was 91.3% for N0, 83.5% for N1, 72.9% for N2 and 56.1% for N3. Pair wise comparison by lymph node status showed that when comparing node-negative with node-positive tumor regardless of tumor size, there was a significant difference in OS ($p < 0.001$). However, when comparing N1 with N2, N3 tumor in a large (> 5 cm) size tumor, there was no significant difference in OS (N1 vs. N2; $p = 0.856$, N1 vs. N3; $p = 0.557$, N2 vs. N3; $p = 0.769$, respectively).

Conclusion: Prognosis of triple-negative breast cancer was not greatly affected by the number of additional positive lymph nodes when tumor size is large (> 5 cm). However, when tumor size is small (≤ 5 cm), there is strong association between number of positive lymph nodes and prognosis.

Poster Discussion

PO08-01

ART THERAPY FOR DEPRESSION IN BREAST CANCER PATIENTS

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[2]College of Art & Human Environment, Konkuk Univ., Korea

Background/Purpose: Depression is not an uncommon condition and may occur at different times through life. Recent research shows that almost every second woman with breast cancer is depressed or has anxiety; the risk for younger women is even higher. Many patients may find that they become depressed because of the impact of breast cancer and this can happen at any stage during diagnosis and treatment, and /or after treatment has finished

Methods: The six patients, aged from 42 to 58 who suffer from postoperative chemotherapy and postoperative trauma which result in emotional instability and anxiety, were enrolled this study.

Results: First, we evaluate the level of stress of patients in relation with to therapy by the stress scale. Second, we evaluate the level of stress of patients by drawng 'a person in the rain.' Third, we evaluate the level of stress of patients by checking serum cortisol level. Through the result of this study, we suggest the benefit of art therapy that can reduce depression in relation with breast cancer

Conclusion: We suggest a future study to prove the efficacy of supportive art therapy in breast cancer patients.

PO08-02

PATIENT SATISFACTION WITH CARE DELIVERED BY ADVANCED PRACTICE NURSES IN KOREA

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Background/Purpose: The purpose of this study was to investigate the patient satisfaction with care delivered by Advanced Practice Nurses (APNs) in Korea.

Methods: The patients who received care by APNs over three times were asked to complete a self-administered patient satisfaction survey designed specially to assess satisfaction with APN's care. The patient satisfaction was categorized into 3 dimensions (attentiveness, comprehensive care and role clarity) 13 items and 1 overall evaluation item. Data collection was performed in a single institution from August 15 to October 31 2009. The 255 subjects were analyzed using descriptive statistics and Friedman test.

Results: The mean score of patient satisfaction with care delivered by APNs was 3.53 out of the highest score 4. Scores on 3 dimensions indicated that patients were satisfied with attentiveness (mean ± SD = 3.59 ± 0.46), comprehensive care (mean ± SD = 3.53 ± 0.52) and role clarity (mean ± SD = 3.319 ± 0.63). The 3 dimensions of satisfaction score were statistically significant by the Least Significance Difference test ($F = 27.20$, $p < 0.0001$). The highest satisfied item was 'APNs was friendly to me' (mean = 3.77). The lowest satisfied item was 'I was clear about how APNs' role is different from a Doctor's role' (mean = 3.18) and 'APNs gave me information about resource utilization (for example, other medical team and a welfare agency to help me) (mean = 3.18).

Conclusion: This study indicates that the patients were satisfied with APNs' activities positively. For better development, APNs have to improve their activities by patient satisfaction evaluation continuously.

Poster Discussion

PO08-03

PARENTING STRESS, PARENTAL BEHAVIORS AND NEEDS OF PARENTS EDUCATION BY CHILDREN CHARACTERISTICS AMONG YOUNGER WOMEN WITH BREAST CANCER

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Background/Purpose: This study was to explore the parenting stress, parental behaviors and needs of patient education by children characteristics among younger women with breast cancer.

Methods: The subjects were 110 younger women with breast cancer (mean age: 42.7 years) who were eligible and agreed to participate in this study. By the use of the questionnaire, a collection was made of data on subjects' demographic characteristics, parenting stress, parental behaviors and needs of patient education. Data were analyzed using SAS program and frequency, mean (SD), t-test, ANOVA and Pearson correlation coefficients were used.

Results: The younger women with breast cancer had high needs of parents education, but their needs were not well met. Patients who have daughter had higher level of needs of parents education related to breast cancer than those who have son., there were a negative correlation in the correlation between the parenting stress and parental behaviors, parenting stress and needs of parents education.

Conclusion: As a result, the development and application of parent education program for mothers with breast cancer in the future should be considered with the demographic characteristics, the social and cultural environment, parenting stress, and parental behaviors of parents and children.

PO08-04

CONSTRUCTS OF COPING AND ADJUSTMENT IN COUPLES WITH BREAST CANCER

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Background/Purpose: The incidence of breast cancer in Korea has been increasing every year, yet little has been revealed about couples' experiences or how dyads interact in order to cope throughout the course of the disease. Since a cancer patient and her or his family are the unit of care, this study aimed to explore the experiences of women and their spouses with breast cancer.

Methods: A descriptive design was utilized. Fourteen participants of seven dyads were recruited from a breast clinic in a university hospital in Seoul. Women who were married, diagnosed with primary breast cancer were included with their husbands. Interviews with each couple were conducted using five key questions in a private room. Audio-recorded data were analyzed by content analysis methods with inductive coding.

Results: While going through the breast cancer event, women focused on 'Controlling and protecting myself', became more assertive to develop their own voices and to take charge of their lives. The husbands prioritized the survival of their wives and became a caring person by 'Reforming my life to care for her'. The couples coped with cancer by 'Working to survive the reality', and they found values and meanings from the cancer experience worth it. However, they were still 'Suspended by unresolved issues without solution', as struggling with sexual changes, depression, fear, burden, and hardships in supporting.

Conclusion: Understanding of couples' lives after breast cancer diagnosis should be incorporated in oncologic nursing care. Educational counseling interventions are needed to empower the dyads to cope with the cancer event successfully.

Poster Discussion

PO08-05

USE OF A SUPERABSORBENT DRESSING TO CONTROL COPIOUS DERMATOLOGICAL METASTASIS IN WOMEN WITH BREAST CANCER

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[1]*Department of Nursing, Yao Municipal Hospital, Japan*
[2]*Department of Breast Surgery, Yao Municipal Hospital, Japan*

Background/Purpose: Cost-effective wound management must take into account the cost of dressings, period of healing and smell management. Uncontrolled exudates consume resources, add to increased physical damage, and impact wound healing. Patients report failure of absorbent wound dressings and resort to products not formulated for wound care, such as diapers with or without the usual absorbent dressings.

Methods: A case series of five patients with copious amounts of drainage and history of periwound adhesive related dermatological metastasis requiring twice a day using form dressings, were placed on a new superabsorbent non-adhesive dressing for two month. Patients continued with their compression requirements included the number of dressing changes, pain, smell, and periwound skin condition.

Results: All patients had a reduction in wound dressing changes to a maximum of once daily (mean1.7days; range 1-3days). Periwound maceration was improved in two patients and resolved in three. All patients reported no wound pain on removal. All patients were able to maintain compression. There were no episodes of periwound adhesive denudations.

Conclusion: Use of a superabsorbent non-adhesive wound dressing can reduce costs in home wound care. Nurses must contemplate to handle wound care and also consider patients whose dressings are not covered under their insurance as dressing frequencies are reduced. Other potential cost savings can be achieved with reduced periwound maceration and trauma.

PO08-06

FACTORS RELEVANT TO UPPER EXTREMITY FUNCTIONS AND HEALTH RELATED QUALITY OF LIFE IN WOMEN AFTER BREAST CANCER SURGERY

Chie Furukawa[1], Yasue Kashiyama[1], Takashi Morimoto[2], Takashi Nomura[2], Ikuharu Morioka[3]

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[2]*Department 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 69 patients after breast cancer surgery who signed informed consent forms at a municipal hospital in Osaka, Japan. Data were gathered by interviewing. The upper extremity functions were evaluated by DASH (JSSH; 30 questions). HRQOL was evaluated by QOL-ACD-B (21 questions). The research was conducted before the previous day of surgery, on the discharge day, 4-week, 12-week and 150-day after surgery (± 7-day). The questionnaire included age, operation method, radiotherapy, chemotherapy and support person status, etc.

Results: All participants were women. The average age was 61.3 years. The scores of DASH and HRQOL did not show significant difference between the young group (less than 60 years old) and the aged group. The scores by the operation method (mastectomy vs. breast- conserving surgery) also showed no significant difference. As to radiotherapy and chemotherapy, treated groups indicated declined score of HRQOL at 150-day after surgery, but the difference was not significant. The 13 women lived without support persons. The scores of DASH and HRQOL in women without support person subsequently remained low (Fig. 1).

Conclusion: The nurses need to support the patients under radiotherapy and chemotherapy around 150-day after surgery. These results suggested nurses also need to support to the participants especially without support person.

Poster Discussion

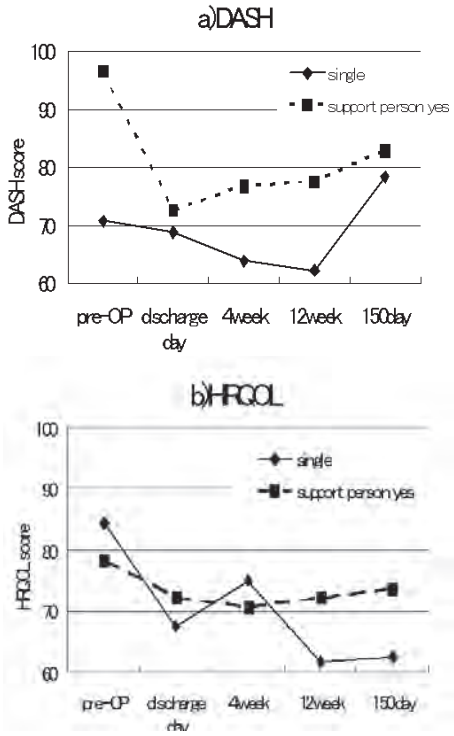

Fig. 1 Trend in DASH and HRQOL of the group by the support person status.

PO08-07

EVALUATION OF ONLINE HEALTH INFORMATION FOR BREAST CANCER PATIENTS IN KOREA

Min Hye Im, So Hyun Park, Min Sun Nam, Min Jae Bing, Soo Jin Yang, Hyun Ju Hwang

The Graduate School of Nursing, Yonsei Univ., Korea

Background/Purpose: As the internet continues to grow and develop, online health information is now one of the most important methods for cancer patients seeking health information. The purpose of this study was to evaluate the quality of online health information accessed by breast cancer patients in Korea.

Methods: As a method, descriptive design was used for this study. For sampling, the 2011National Customer Satisfaction Index, five tertiary hospitals, two national institution's websites, and sixty websites from three Korean portal sites were selected. Data were analyzed with a modified DISCERN (Charnock et al., 1999) for evaluating online health information.

Results: The results showed significant differences in the quality of the health information provided. The credibility and the overall quality of online health information provided by various sources is indicatedinthe following order: National institution (4.8) > nonprofit organization (4.6) > tertiary hospital (4.1) > medical bulletin boards (for counseling) (3.1) > private medical clinics (2.3) > private online blogs (1.8) > commercial web site related to healthy food consumption (1.1).

Conclusion: In Korea, the quality and credibility of online health information focused on breast cancer varies according to the information provider. Health care providers should monitor the online health information available to reach the public at their level of knowledge. For health information consumers, education programs should be guided toward evaluating the online information to meet consumers' unmet need for knowledge regarding breast cancer and cancer management.

PO08-08

LITERATURE REVIEW OF THE STIGMA OF BREAST CANCER

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Background/Purpose: The stigma of breast cancer could have a profound impact on treatment and survival. Clinicians need to have a better understanding of the stigma reflecting culture surrounding breast cancer because immigrants and people from different cultures are increasing. The purpose of this study was to review the stigma associated with breast cancer.

Methods: A systematic literature review was conducted. Literature published between 1994 and 2011, focusing on the stigma of breast cancer was collected from the PubMed, CINAHL, Wiley online library, and Web of Science databases. The search terms used were breast cancer and stigma, breast malignancy and stigma, and breast neoplasm and stigma. We reviewed 30 studies.

Results: The following 5 main categories described in the literature were included: (1) fatalism described as "bad luck (bad card)," "regarded as the prophecy of death," and "your destiny," (2) religion described as "God tests our patience," "not living according to the religion's commandments," and "God's grace," (3) genetics described as "family mutant" and "their daughters may not be chosen for marriage," (4) sexuality described as the "loss of femininity, sexual attraction, and sexual pleasure" and "a woman without a breast is not a woman," and (5) social interactions described as "concealment of the illness."

Conclusion: Our review showed that women from various countries and ethnic backgrounds share similar views regarding the stigma of breast cancer. The aforementioned stigmas should be considered while raising the awareness of breast cancer.

PO08-09

ACTIVITIES OF SELF-HELP GROUPS FOR BREAST CANCER PATIENTS IN KOREA

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Background/Purpose: Joining a self-help group is one of the positive strategies that breast cancer patients can employ to promote quality of life. The purpose of this study was to describe the activities of self-help groups for breast cancer patients in Korea.

Methods: A descriptive study design was used. A convenient sampling method was applied, and eight popular self-help groups in urban area were selected. Their activities were described in terms of structure, process, and outcome of each self-help group. With "Evaluation Criteria for Internet Cancer Support Groups" (Im et al. 2010), five additional online self-help communities were analyzed.

Results: The characteristics of the eight self-help groups were as follows: Seven were affiliated with major hospitals; the eighth was not affiliated with a hospital. The activities of the eight self-help groups were diverse. There were community-based groups and professionally led groups. The number of meetings ranged from meetings that had no specific regularity to weekly or quarterly meetings. Four of the self-help groups consisted of only breast cancer patients and no health care providers. The interests and activities of the small groups included choir, walking outdoors, dancing, and so on. The five online self-help communities were also analyzed. The target users were breast cancer patients and their families. The purpose of the online communities was to support patients and share information.

Conclusion: In Korea, there is a wide range of self-help groups for breast cancer patients operating with and without hospital affiliation. All of these groups help patients and share information.

PO08-10

CLINICAL PSYCHOLOGICAL INTERVENTION TO BREAST CANCER WOMEN WITH PSYCHOLOGICAL DISTRESS

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[4]*Graduate School, Mukogawa Women's Univ., Japan*

Background/Purpose: The purpose of this study is to clarify effective interventions by a clinical psychologist to breast cancer patients with psychological distress.

Methods: The persons were composed of 18 women who were diagnosed breast cancer. The interventions were conducted by patients' or medical doctors' request. Intervention method was unstructured one-on-one interview. Each interview was usually no more than 60 minutes.

Results: Age varied within a wide range (40-73 years). The cases were classified as following (1) the cases with the mean number of 14.1 interviews were conducted to 8 patients to reduce anxiety at the progressive-relapse-stage. The number of these interventions tended to increase, because of continuous interventions for the patients at this stage. (2) The cases with the mean number of 3.4 interviews were conducted to 7 patients to reduce sudden mental shock due to disclosure a diagnosis of breast cancer, pre-surgical anxiety, and relapse. The interventions tended to end in short-term critical care intervention. (3) The cases with the mean number of 2.7 interviews were conducted to 3 patients requested to receive medical treatment by psychiatrists. The interventions tended to end in short-term approaches, because of the cases having been transferred to the psychiatrists.

Conclusion: This study suggested effective interventions to the breast cancer women by a clinical psychologist. The roles of the psychological interventions were classified into two: first, to assess properly, and second, to interview purposefully as one of medical team members.

PO08-11

PSYCHOSOCIAL DISTRESS AND QUALITY OF LIFE IN CANCER PATIENTS

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Background/Purpose: The purpose of this research was to survey the level of distress in cancer patients and assess their needs for nursing intervention to decease it.

Methods: We surveyed the level of distress and assessed the need of distress nursing intervention using 242 cancer patients in one general hospital. Data were collected from September 13 to October 22, 2010.

Results: 55.3% of patients (DT ≥ 4) experienced clinically significant level of psychosocial distress. Patients who described higher distress level reported fatigue/physical weakness, concerns about their health, failure of memory, depression, fear, and sleep problems. Among the general and illness related characteristics of subjects, financial compensation, family history of gynecologic cancer, illness stage and cancer recurrence were related to the psychosocial distress. The mean score of quality of life was 3.36 (total 5 score). Among the general and illness related characteristics of subjects, job, marital status, educational status, monthly family income, financial compensation, time of diagnosis, illness stage and cancer recurrence were related to the quality of life. The psychosocial distress and quality of life was negatively correlated ($r = -0.576$, $p < 0.001$).

Conclusion: The results of the study indicated that the cancer patients had higher psychosocial distress than general population. Thus oncology professionals need to pay attention to cancer patients, by regularly assessing their psychosocial distress and by providing appropriate psychosocial intervention to improve their quality of life.

Poster Discussion

PO08-12

A META-ANALYSIS OF INTERVENTION STUDIES ON NAUSEA AND VOMITING IN CANCER PATIENTS

Pok-ja Oh, Ji Hyun Yoo

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Background/Purpose: This study was to analyze the characteristics and effect size of intervention studies applied to nausea & vomiting of cancer patients.

Methods: For meta-analysis, a total of 1,083 studies were retrieved from search engine. And 20 studies published to 2010 were selected upon their satisfaction with the inclusion criteria with a total of 698 participants. Two authors independently extracted data from the selected studies and assessed the methodological quality. The data was analyzed by the RevMan 5.0 program of Cochrane library.

Results: 1) Intervention studies included 9 studies on acupuncture (45%), 5 for massage (25%), 2 for oral cryotherapy (10%) and 4 others therapy. 2) The effect size of the intervention studies shown higher effect size in order of massage (d = -1.62) and acupuncture (d = -0.89).

Conclusion: This study suggest that non-drug therapy can reduce the levels of nausea and vomiting intensity, even though the number of intervention studies and randomized controlled trials are very rare.

PO08-13

ACTIVE COUNSELING ABOUT FERTILITY PRESERVING FOR BREAST CANCER PATIENTS RECEIVING SYSTEMIC THERAPY

Noriko Okada, Tadahiko Shien, Yuko Tsuyumu, Takayuki Motoki, Naruto Taira, Jyunji Matsuoka, Hiroyoshi Doihara

Breast Cancer Treatment and Reconstruction Center, Okayama Univ. Hospital, Japan

Background/Purpose: In Japan, young breast cancer (BC) patients who can get pregnant are getting more. On the other hand systemic therapies for BC are improved and become more effective and longer. We investigated to made effective consulting system to preserve fertility of young BC patients receiving systemic therapy in this study.

Methods: We asked questionnaire about pregnancy, consulting and fertility issues directly to young BC patients who want a new child when they start BC treatment. According to these results, we practically started the active counseling to young BC patients.

Results: Eighty percents women who want a child were married and 40% women had a child before treatment. 75% women wanted to receive counseling with their husband or partner. They thought that their life is more important than making a new child before starting treatment. However after treatment they could think calmer about importance of their fertility.

Conclusion: We started counseling about fertility on the time changing or starting new treatment and explaining about total treatment schedule and prognosis. 20% young BC patients wanted to preserve fertility. We thought that more frequent talks with them are necessary for effective fertility preserving.

PO08-14

EVALUATION OF STRUCTURED EDUCATION PROGRAMS FOR BREAST CANCER PATIENTS IN KOREA

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The Graduate School of Nursing, Yonsei Univ., Korea

Background/Purpose: To manage breast cancer patients' symptoms and promote a higher quality of life for them, one of intervention strategies is structured education programs. These are generally implemented in hospitals where breast cancer patients receive mastectomies and chemotherapy. The purpose of this study was to describe the status of such programs for breast cancer patients in Korea.

Methods: The study used a descriptive design and a convenience sample taken from structured education programs in six university affiliated hospitals in Korea. Descriptive analysis was performed in terms of educational structure and process including operator, frequency, and contents.

Results: Most of the structured education programs studied were operated either weekly or semiweekly for 60-120 minutes by a physician and/or nurse/advanced practice nurse. Most of the six hospitals provided these programs for free but two charged registration fees. The most widely used educational method was lecture. The educational contents comprised seven categories: disease, post-operative management, chemotherapy, radiation therapy, diet education, rehabilitation and symptom management, and psychological and social issues. Doctors, nurses, and related health care professionals provided patient education in these areas.

Conclusion: Most hospitals where breast cancer patients receive care provide structural education programs. This study highlighted important considerations for developing program evaluation methods. Future research should evaluate such structured education programs in terms of structure, process, and outcome.

PO08-15

ATTITUDE TOWARD MENOPAUSE, MENOPAUSAL SYMPTOM AND QUALITY OF LIFE IN PREMENOPAUSAL BREAST CANCER PATIENTS

Sunyoung Park[1], Moon-hee Gang[2], Young-hee Park[1], Mi-young Sung[1], Eun-jung Song[1], Eil-sung Chang[1], Je-ryong Kim[1], Jin-sun Lee[1]

[1]*Department of Surgery, Chungnam National Univ. Hospital, Korea*
[2]*College of Nursing, Chungnam National Univ., Korea*

Background/Purpose: The purpose of this study was to identify the attitude toward menopause, the menopausal symptom, and the quality of life and to examine the relationship among the attitude toward menopause, the menopausal symptom, and the quality of life in premenopausal breast cancer patients.

Methods: A descriptive correlational study design was used. Participants were 68 premenopausal breast cancer patients from C Hospital. Data were collected on July 1-20, 2011 using self-administered questionnaires, and analyzed using the SPSS/WIN 12.0.

Results: The menstrual morbidity was experienced 85.6% in the subjects including 19.1% of the menstrual irregularity and 76.5% of menopause. Subjects have positive attitudes on the menopause and moderate level of menopausal symptom. The attitude toward menopause, the menopausal symptom, and the quality of life were found to be significantly positively correlated with one another.

Conclusion: Findings of this study allow a comprehensive understanding of the attitude toward menopause, the menopausal symptom, and the quality of life in premenopausal breast cancer patients. Further study with larger random sample and various variables is necessary.

PO08-16

EFFECTS OF BEHAS EXERCISE PROGRAM ON GROUP COHESION, CANCER COPING, EXTERNAL ROTATION IN BREAST CANCER PATIENTS

Sunyoung Park[1], Sun Ae Kim[2], Shin Hong Min[3], Jong Im Kim[3]

[1]*Department of Surgery, Chungnam National Univ. Hospital, Korea*
[2]*Department of Nursing, Kkottongnae Univ., Korea*
[3]*College of Nursing, Chungnam National Univ., Korea*

Background/Purpose: The purpose of this study was to identify effectiveness of a BeHaS exercise program that consists of exercise, education, and cognitive supports to improve group cohesion, cancer coping, external rotation in breast cancer patients.

Methods: A one group pre-post test design was conducted on breast cancer patients from C Hospital. Thirty patients were recruited and participated in BeHaS exercise program for 120 minutes per session once a week for 10 weeks. Data were collected from May to July 2011 using self-administered questionnaires. And outcome measures were group cohesion, cancer coping, external rotation. SPSS/WIN 12.0 was used for the data analysis.

Results: The mean age of participants was 53.7 and the mean period after the surgery was 12.93 months. There were significant differences in the group cohesion, cancer coping, the external rotation of affected arm and that of unaffected arm between pretest and posttest.

Conclusion: Findings of this study confirmed that BeHaS exercise program was proved to be an effective nursing intervention for improving breast cancer patient's group cohesion, cancer coping, external rotation. Further studies are needed to find another effects of BeHaS exercise program for health promotion of breast cancer patients.

PO08-17

FACTORS INFLUENCING SLEEP PATTERN IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY

Hyang Sook So[1], Myeong Jeong Chae[2], Ji Eun Hong[1], Ji Youn Jung[1], Young Ran Kwon[1], Yu Hyoung Kim[1], Ju Young Kim[1], Ji Young Kim[1]

[1]*College of Nursing, Chonnam National Univ., Korea*
[2]*Christian College of Nursing, Korea*

Background/Purpose: The purpose of this study was to identify factors influencing quality of life after analyzing the relationship between 3 factors of sleeping disturbances and quality of life in hospitalized chemotherapy patients.

Methods: The subject of this study were eighty four cancer patients who underwent chemotherapy at a university hospital. Research tools were sleep pattern scale (Oh, 1998), MDA (M.D. Anderson Symptom Inventory) Symptom Inventory-K (Yoon, 2006), Environmental disturbing factor scale (Paik, 2000), depression scale (Zung, 1965). The collected data was analyzed with the SPSS program which was used for descriptive statistics, simple correlation and hierarchical multiple regression.

Results: There were no differences between the score of sleep pattern and any general characteristics. But group who took a sleeping pills was showed low score of sleep pattern ($t = -3.568$, $p = 0.001$). There were statistically significant relationships between symptom cluster ($r = -0.540$, $p < 0.001$), envi -ronmental factor($r = 0.354$, $p = 0.001$), depression ($r = 0.437$, $p = 0.001$) and sleep pattern. The significant influencing factors on sleep pattern were symptom cluster ($\beta = -0.444$, $p < 0.001$), depression ($\beta = -0.444$, $p < 0.001$), cycles of chemotherapy ($\beta = -0.193$, $p = 0.024$), and taking of sleeping pill ($\beta = -0.185$, $p = 0.030$). The total variance explained the score of sleep pattern was 51.4%.

Conclusion: Cancer patients experienced physical symptom cluster and sleep disturbance which led to negative effect on quality of life. Non-pharmacological nursing intervention for relieving physical symptom cluster and improving sleep pattern need to develop and apply at cancer nursing units.

Poster Discussion

Table 1. Differences of Sleep Pattern according to Characteristics

(N=84)

Characteristics	Group	No.	Sleep Pattern	
			M±SD	t or F-test (p)
Age(yrs)	22-54	29	36.7±5.5	.937 (.396)
	55-64	21	34.4±6.2	
	65-84	34	35.8±5.5	
Gender	Men	39	36.7±5.3	1.485 (.141)
	Women	45	34.9±5.9	
Types of Cancer	Colorectal	43	36.0±5.2	1.512 (.218)
	Stomach	17	37.1±5.4	
	Gynecological	11	36.1±7.2	
	Breast	13	32.8±6.0	
Caregiver	Have	53	35.9±6.1	.222 (.825)
	Have not	31	35.6±4.9	
Cycle numbers of chemotherapy	1-3	21	36.7±5.1	1.044 (.357)
	4-6	30	36.3±5.3	
	7-48	33	34.7±6.3	
Taking Sleeping Pill	Do	13	30.9±4.9	-3.568 (.001)
	Do not	71	35.6±4.9	

Table 1.

Table 2. Relationships between Sleep Pattern and Factors of Sleep Disturbance

(N=84)

	Factors of Sleep Disturbance			Sleep Pattern
	Physical Symptoms	Depression	Environmental Factor	
	r (p)	r (p)	r (p)	r (p)
Physical Symptoms	1			
Depression	-.132 (.233)	1		
Environmental Factor	-.306 (.005)	.255 (.019)	1	
Sleep Pattern	-.540 (<.001)	.437 (<.001)	.354 (.001)	1

Table 2.

PO08-18

FACTORS INFLUENCING QUALITY OF LIFE IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY

Hyang Sook So[1], Myeong Jeong Chae[2], Gyung Ae Chung[3], Ji Youn Jung[4], Ji Eun Hong[1]

[1]*College of Nursing, Chonnam National Univ., Korea*
[2]*Christian College of Nursing, Korea*
[3]*Department of Nursing, Chonnam National Univ. Hwasun Hospital, Korea*

Background/Purpose: The purpose of this study was to identify factors influencing quality of life after analyzing the relationship between 3 factors of sleeping disturbances and quality of life in hospitalized chemotherapy patients.

Methods: The subject of this study were eighty four patients who had colorectal, gastric, gynecologic, and breast cancer and recruited from cancer center of a university hospital. A questionnaire consisting of sleep pattern scale (Oh, 1998), MDA (M.D. Anderson Symptom Inventory) Symptom Inventory-K (Yoon, 2006), Environmental disturbing factor scale (Paik, 2000), depression scale (Zung, 1965), and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30 (Yoon, 2004) was given. The collected data was analyzed with the SPSS program which was used for descriptive statistics, pearson correlation coefficients and hierarchical multiple regression.

Results: There were no differences between the score of quality of life and any general characteristics. But group who took a sleeping pills was showed low score of quality of life ($t = -3.563$, $p = 0.001$). There were statistically significant relationships between sleep pattern ($r = 0.524$, $p < 0.001$), symptom cluster ($r = 0.571$, $p < 0.001$), general health status ($r = 0.319$, $p = 0.003$) and quality of life. The significant influencing factors on quality of life were symptom cluster ($\beta = -0.421$, $p < 0.001$), sleep pattern ($\beta = 0.228$, $p = 0.030$), taking of sleeping pill ($\beta = -0.208$, $p = 0.021$), and accompany with spouse ($\beta = 0.203$, $p = 0.015$). The total variance explained the score of quality of life was 47.4%.

Conclusion: Cancer patients experienced physical symptom cluster and sleep disturbance which led to negative effect on quality of life. Non-pharmacological nursing intervention for relieving physical symptom cluster and improving sleep pattern need to develop and apply at cancer nursing units.

Poster Discussion

Table 1. Differences of Sleep Pattern according to Characteristics

(N=84)

Characteristics	Group	No.	Sleep Pattern	
			M±SD	t or F-test (p)
Age(yrs)	22~54	29	36.7±5.5	.937 (.396)
	55~64	21	34.4±6.2	
	65~84	34	35.8±5.5	
Gender	Men	39	36.7±5.3	1.485 (.141)
	Women	45	34.9±5.9	
Types of Cancer	Colorectal	43	36.0±5.2	1.512 (.218)
	Stomach	17	37.1±5.4	
	Gynecological	11	36.1±7.2	
	Breast	13	32.8±6.0	
Caregiver	Have	53	35.9±6.1	.222 (.825)
	Have not	31	35.6±4.9	
Cycle numbers of chemotherapy	1~3	21	36.7±5.1	1.044 (.357)
	4~6	30	36.3±5.3	
	7~48	33	34.7±6.3	
Taking Sleeping Pill	Do	13	30.9±4.9	−3.568 (.001)
	Do not	71	35.6±4.9	

Table 1.

Table 2. Relationships between Sleep Pattern and Factors of Sleep Disturbance

(N=84)

	Factors of Sleep Disturbance			Sleep Pattern
	Physical Symptoms	Depression	Environmental Factor	
	r (p)	r (p)	r (p)	r (p)
Physical Symptoms	1			
Depression	−.132 (.233)	1		
Environmental Factor	−.306 (.005)	.255 (.019)	1	
Sleep Pattern	−.540 (<.001)	.437 (<.001)	.354 (.001)	1

Table 2.

PO08-19

FACTORS OF SLEEP DISTURBANCE AND SLEEP PATTERNS AMONG CANCER CHEMOTHERAPY PATIENTS

Hyang Sook So[1], Myeong Jung Chae[2], Ji Eun Hong[1], Ji Youn Jung[1], Young Ran Kwon[1], Yu Hyoung Kim[1], Ju Young Kim[1], Ji Young Kim[1]

[1]*College of Nursing, Chonnam National Univ., Korea*
[2]*Christian College of Nursing, Korea*

Background/Purpose: The purpose of this study was to identify sleep pattern and factors of sleep disturbance (symptom cluster, environmental factor, depression) of the hospitalized chemotherapy patient.

Methods: The subject of this study were 84 people who underwent chemotherapy, had colon cancer, gastric cancer, gynecologic cancer, breast cancer, and recruited from cancer center of a university hospital. Data was collected from July 4th to 15th, 2011. A questionnaire consisting of sleep pattern scale (Oh, 1998), MDA (M.D. Anderson Symptom Inventory) Symptom Inventory-K (Yoon, 2006), Environmental disturbing factor scale (Paik, 2000), Self rating depression scale (Zung, 1965) was given. The collected data was analyzed with the SPSS program which was used for descriptive statistics, pearson correlation coefficients.

Results: The major findings of this study were as follows : There was no difference between sleep pattern and age, gender, diagnosis, number of admission, types of bed room, and presence or not of spouse and caregiver. But group who took a sleeping pills was showed low score of sleep pattern ($t = -3.568$, $p = 0.001$). The mean scores of sleep pattern, symptom cluster, environmental factor, and depression were 35.8 ± 5.7, 68.2 ± 38.7, 58.2 ± 7.9, 50.9 ± 5.2 respectively. There were significant relationships between symptom cluster ($p < 0.001$), environmental factor ($p = 0.001$), depression ($p < 0.001$) and sleep pattern.

Conclusion: Most of the hospitalized cancer chemotherapy patients reported sleep disturbance. There were especially significant relationships between sleep pattern and physical symptom cluster, inpatient environmental factors, and depression for used of the chemotherapy. In the future, nursing interventions for relieving physical symptom, preventing depression, and preparing nice environment need to be established.

Poster Discussion

Table 1. Differences of Sleep Pattern according to Characteristics

(N=84)

Characteristics	Group	No.	Sleep Pattern	
			M±SD	t or F-test (p)
Age(yrs)	22~54	29	36.7±5.5	.937 (.396)
	55~64	21	34.4±6.2	
	65~84	34	35.8±5.5	
Gender	Men	39	36.7±5.3	1.485 (.141)
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	Breast	13	32.8±6.0	
Caregiver	Have	53	35.9±6.1	.222 (.825)
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Cycle numbers of chemotherapy	1~3	21	36.7±5.1	1.044 (.357)
	4~6	30	36.3±5.3	
	7~48	33	34.7±6.3	
Taking Sleeping Pill	Do	13	30.9±4.9	−3.568 (.001)
	Do not	71	35.6±4.9	

Table 1.

Table 2. Influencing Factors on Sleep Pattern

(N=84)

Sleep Pattern	B	SE	β	p	R^2	F	p
Constant	20.445	4.738		<.001	.514	20.871	<.001
Physical Symptoms	−.065	.012	−.444	<.001			
Depression	.419	.091	.383	<.001			
Cycle numbers of chemotherapy	−.141	.061	−.193	.024			
Taking Sleeping Pill	−2.881	1.303	−.185	.030			

Table 2.

PO08-20

INTRODUCTION OF PEER SUPPORT PROGRAM FOR BREAST CANCER PATIENTS

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Background/Purpose: Peer support and the integration of peer relationship in the provision of health care are concepts of substantial significance to medical professionals today. We have introduced Peer Support Program for Breast cancer patients that incorporate peer relationships into support-enhancing intervention since 2009. The purpose of the current report was to describe the activities of the Peer-Support Program for Breast cancer patients in Okayama University Hospital.

Methods: Ten cases which used the program were examined from the aspect of their recruit, support contents and outcomes.

Results: Three patients applied to the program by themselves. They had a strong sense of purpose to request peer support and they were given appropriate support suitable for their needs. On the other hand, 7 patients were recommended to receive peer support from medical professionals. They needed various kinds of information based on peer's practical experience in order that they made a choice of their treatment with final decision. All of 10 cases accepted their treatment that they had choice by themselves. And peer supporters also made an emotional impact on them.

Conclusion: Peer support satisfied breast cancer patient's needs. Peer support had an essential role to improve quality care and health outcomes. For diverse patient's needs ,we have to refine this program.

PO08-21

WHAT DO WOMEN WITH BREAST CANCER NEED TO LIVE AFTER THEIR OPERATION? VIEWS OF BREAST CANCER PATIENTS IN JAPAN

Takako Yamamoto

President, Breast Cancer Network Japan, Japan

Background/Purpose: For Japanese women who have had the breast cancer operation, it is important to have reassurance that they can live healthily and happily again after their cancer experience. They try to talk to doctors, and also get information from books and the internet. However, their concerns cover a wide range of issues and information cannot be found in only one place. Furthermore, information is only part of their recovery process. Japanese breast cancer patients still have unmet needs in terms of recovery.

Methods: For over 30 years, the Breast Cancer Network Japan has provided support to breast cancer patients to help them live again after their operations. In 2011, we began conducting a survey of our 3000+ members to ask them "what do women with breast cancer need to live after their operation?" The results will help to identify patients' needs, including what types of support and information they want and the best way to get them.

Results: Preliminary results suggest that doctors are too busy to satisfy patients' needs. Many patients use books or the internet for information, but these are one-way-communication. Many patients want to talk to someone who underwent the same experience, so that they can share their feelings of fear, uncertainty about treatment, how to deal with their families, and other anxieties about their future.

Conclusion: Cancer support groups should play a critical role in supporting cancer patients and must cooperate with other groups such as doctors and the media to promote recovery.

PO09-02

AN INTERNATIONAL PERSPECTIVE: THE ROLE OF NURSE INVOLVEMENT IN IMPROVING BREAST CANCER CONTROL

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Background/Purpose: Non-Western, non-Caucasian populations comprise 90% of the world's estimated 3.2 billion women, living mostly in low and middle income nations. While medical advances have greatly reduced breast cancer morbidity and mortality in developed nations, those are on the rise in many low and middle income nations. The purpose of the study was to identify emerging needs and challenges observed by breast cancer thought leaders in diverse regions of the world consisting mainly of lesser developed nations to identify strategies for improving breast cancer control.

Methods: Two hundred twenty-five breast cancer medical, advocacy and policy leaders from 30 countries in Latin America, Asia, the Middle East/North and South Africa, Canada and Australia participated in this study. The study sample was composed of 203 breast cancer specialists, 12 patient advocates and 10 policy makers.

Results: The most salient needs and challenges identified were to: (1) develop nurses trained in breast cancer patient and family care, management, education and clinical research (48%); (2) individualize breast cancer therapy (47%); and (3) improve understanding of the reasons for apparently higher proportions of younger women presenting with more aggressive tumors among these predominantly non-Caucasian populations (45%). Analysis of these and other needs identified evolved into 4 key themes and sub-dimensions involving nurses to improve breast cancer control: Capacity, Research, Advocacy and Access.

Conclusion: The most significant need identified by this study was to increase both the capacity and capability of breast cancer nurses. A comprehensive approach to doing this would include: (1) increasing capacity to educate nurses in breast cancer patient education and related care issues in nursing schools and teaching hospitals; (2) working with local medical societies, educational institutions and governmental authorities to enable nurses to work as primary care practitioners; and (3) increasing participation of nurses in breast cancer clinical research, working with clinicians and in collaboration with breast cancer research centers of excellence from around the world.

PO09-03

MULTIDISCIPLINARY TEAM APPROACH IN BREAST CANCER: A NATIONWIDE SURVEY IN KOREA

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Background/Purpose: This assesses current working of multidisciplinary team (MDT) meetings across the Korea through surgeons' reports and their current commitments to MDT meetings pertaining to breast cancer, and to determine any perceived areas of potential improvement.

Methods: From December 2008 to February 2009, a questionnaire was sent to 307 members of Korean Breast Cancer Society. From December 2008 to February 2009, the survey was distributed by surface and electronic mail, with an initial mailing followed by another distribution to non-responders eight weeks later.

Results: Sixty-five individuals (21.2%) returned the completed survey. Of these, 38 responders (62.3%) participated in MDT meetings. Most (97.4%) breast health specialists regarded MDT meetings as an effective method for treatment planning. Most responders (94.7%) reported that the MDT leader was a breast surgeon. Almost all newly diagnosed patients and most postoperative patients were discussed in MDT meetings. Discussion concerning patients with benign disease was less frequent.

Conclusion: The MDT approach is perceived as an effective method for breast cancer treatment planning and is a feature in most major centers in Korea. Further work is needed to ensure that the MDT approach operates as intended and that all breast cancer patients have access to a MDT.

PO09-04

HEALTH SYSTEM PROFESSIONALS' PERSPECTIVES ON BREAST CANCER PREVENTION AND MANAGEMENT IN PAKISTAN

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Background/Purpose: Breast cancer is a significant public health problem in Pakistan (annual age standardized incidence and mortality of 69.1/100,000 (98-102) and 22/100,000 (95-97) respectively) and presents challenges in terms of public health interventions and health services reorientation needed to tackle the problem. As part of a larger study to identify strategies that can enhance the performance of the health system in Pakistan, this research focuses on interviewing health system professionals and policy makers to explore their perspectives about current and possible approaches to address this public health issue.

Methods: Interviewees, with a background of experience in and association with breast cancer management, health systems management and policy development with regard to chronic disease, were identified through a snowballing sampling methodology. The interviews were semi-structured and recorded. Transcription of the interviews was followed by thematic analysis.

Results: Ten key informants were interviewed. The participants were practicing breast surgeon, oncologists and policy development experts in the government and private sectors. The key informants highlighted issues with regard to community characteristics relevant to early detection and management, screening challenges in the context of Pakistani health system, the policy program translation gap and the potential role of media in increasing awareness.

Conclusion: Breast cancer is recognized as a public health problem in Pakistan at the policy level; however there is an absence of a national policy on the issue. Besides resource constraints lack of demand has also contributed to non-implementation of policy decisions.

PO09-05

INVASIVE DUCTAL CARCINOMA ARISING FROM ECTOPIC BREAST TISSUE IN AXILLA: A CASE REPORT

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Background/Purpose: Primary carcinoma of ectopic breast tissue is rare. Ectopic axillary breast tissue is different from axillary components of the tail of Spence because it develops as a result of failed resolution of the mammary ridge, an ectodermal thickening that extends from axilla to the external genitalia.

Methods: We present a 57-year-old female with large erythematous bulging mass in the right axilla. The initial differential diagnosis was lymphadenitis or infected epidermal inclusion cyst. Imaging studies including positron emission tomography-computed tomography (PET-CT) did not reveal any lesions in other organs except the right axilla. To confirm the diagnosis, core needle biopsy was performed. Pathologic finding suggested invasive ductal carcinoma. Wide excision of the right axillary mass with lymph node dissection was done.

Results: From pathologic findings, breast parenchyme was not found in the specimen, and estrogen receptor, progesterone receptor and C-erb-B2 were negative. However, pathologic finding from permanent sections showed invasive ductal carcinoma and no surrounding lymphoid tissue nor lymphovascular infiltration were found.

Conclusion: Therefore our case is more relevant to primary carcinoma arising from ectopic breast tissue than metastatic carcinoma.

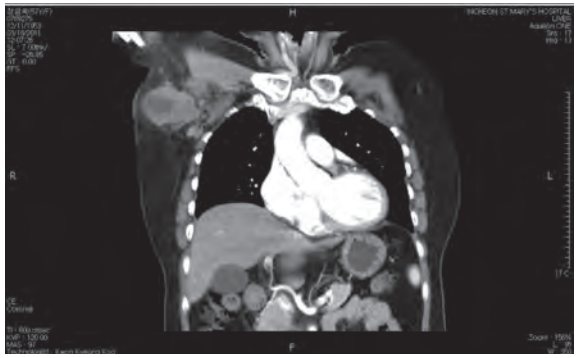

Fig. 1

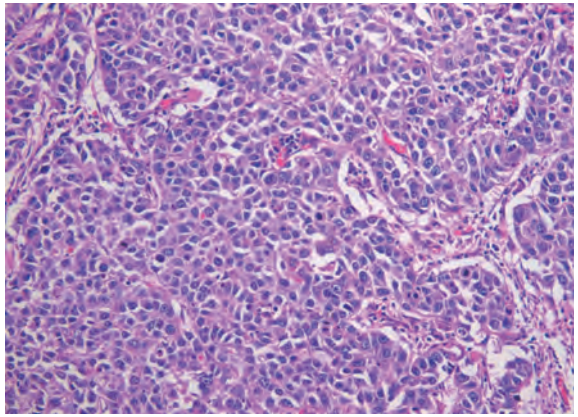

Fig. 2

PO09-06

INVASIVE MYOEPITHELIAL CARCINOMA ARISING IN ADENOMYOEPITHELIOMA: TWO CASES REPORT

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Background/Purpose: Adenomyoepithelioma is mostly benign, malignant change arising in this lesion is not frequent and only a few cases have been reported.

Methods: We report two cases of invasive myoepithelial carcinoma arising in adenomyoepithelioma.

Results: A 51-year-old female who complained a right breast mass was treated by Mammotome at local clinic. Histologic result of lesion was complex fibroadenoma. During follow up the lesion was increased in size. Excisional biopsy was completed and histologic result was invasive myoepithelial carcinoma arising in adenomyoepithelioma. A 44-year-old woman presented a right breast mass that had been palpable for one week. Two years ago, the patient had Mammotome biopsy and pathology showed sclerosing adenosis with fibrocystic change. Recently the patient complained palpable mass at previous biopsy site. Ultrasonogram showed more enlargement mass at previous biopsy site. Core biopsy showed myoepithelial lesion. Wide excision was performed then final histologic result was myoepithelial carcinoma arising in adenomyoepithelioma.

Conclusion: Adenomyoepithelioma is a rare lesion that can involve the breast tissue.

PO09-07

CANCER OF THE ACCESSORY BREAST CANCER: A CASE REPORT

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Background/Purpose: Ectopic breast tissue exists in the 2-6% of the population. Failed resolution of the remaining mammary ridges form ectopic breast tissue. Although ectopic breast cancer has the same development and course as non-ectopic breast cancer, treatment guideline for accessory breast cancer are not enough for its rare incidence. We report our experience of this rare disease.

Results: A 53-year-old female visited women-oncology clinic. For right axillary mass, an excisional biopsy was performed and revealed adenocarcinoma in accessory breast. She had ultrasonograpy and there was normal breast finding and had no significant lesion but fluid collection in the excisional site. And it showed no significant finding in mammography, PET and MRI. She got wide excision around previous excisional site with axillary lymph node dissection. Due to tumor was left in resection margin, it needed more dissection. The tumor size was 1.2 × 1.2 cm (including excised mass) and no metastasis in axillary lymph node. ER/PR/C-erb B2 were revealed positive/positive/negative (1+). She has no perioperative complications. She had chemotherapy with AC (Adriamycin 60 mg/m^2, cyclophosphamide 600 mg/m^2) regimen after operation.

Conclusion: It is hard to diagnose accessory breast cancer early due to its non-typical location. It usually appears bilaterally, so clinicians need to evaluate for counterpart. It has many differential diagnoses (especially with axillary node metastasis of occult breast cancer), so we needed early tissue biopsy. Imaging studies including mammography, PET and MRI also make proper treatment. The patient must have careful follow up for exclude any manifestation of occult breast cancer.

PO09-08

A CASE REPORT OF PRIMARY BREAST ANGIOSARCOMA WITH FATAL PULMONARY RECURRENCE

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Background/Purpose: Primary angiosarcomas of the breast are rare malignancy that account for fewer than 0.04% of all malignant breast tumors. The prognosis is poor. Surgery is the first line of treatment for angiosarcoma. Adjuvant chemotherapy and radiotherapy have been tried, but their efficacy remains controversial.

Methods: This is a case of a 47-year-old woman with a palpable left breast mass that was diagnosed as a primary angiosarcoma. The patient underwent modified radical mastectomy with adjuvant chemotherapy and radiotherapy.

Results: Postoperatively 18 months later, the angiosarcoma recurred. The patient returned complaining of dyspnea and hemoptysis and was found to have a large pleural effusion. She developed a gradual onset of thrombocytopenia that persisted despite platelet transfusions. Finally, the patient died of respiratory failure secondary to pulmonary hemorrhage.

Conclusion: We have detailed our experience with a primary breast angiosarcoma that failed to respond to multimodality treatment of surgical resection and adjuvant chemo- and radiotherapy.

PO09-09

PRIMARY BREAST LYMPHOMA

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Background/Purpose: Primary malignant lymphoma of the breast is very rare disease, accounting for 1.7% to 2.2% of extranodal lymphoma and 0.38% to 0.7% of non-Hodgkin's lymphoma. Among the primary lymphomas, the most common histologic types are the large B-cell diffuse lymphomas and the B mucosa-associated lymphatic tissue lymphomas. Clinically the diagnosis of primary breast lymphoma is often missed, the usual preoperative diagnosis being carcinoma. Radical surgery is to be avoided and radiation therapy with limited surgery provides excellent local regional control.

Methods: We studied 5 cases of primary breast lymphoma in female patients. Clinical data, histologic findings, immunohistochemical reactions, treatment, and clinical follow-up were reviewed.

Results: Average age of the 5 patients were 47 years. The right breast was the most affected, and 1 patient was affected in both breasts. The most common symptoms were the presence of palpable mass and nodes. The clinical course was of 1 to 3 months before diagnosis. Histologically, four primary breast lymphomas were large B-cell lymphomas and 1 patient was unclassifiable malignant lymphoma. Four patients were positive to CD20 and 1 patient was negative to CD20, 2 expressed both bcl2 and bcl6, 2 expressed only bcl2 and 1 expressed only bcl6. Two patients are still alive, and the other was lost during follow-up.

Conclusion: Primary breast lymphomas are very rare disease. The most common histologic type was the large B-cell diffuse lymphoma. Surgical therapy has varied from biopsy to radical mastectomy. Chemotherapy and radiation therapy have been used as adjuvant or primary therapy.

PO09-10

FRACTURE AND EMBOLIZATION OF TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES FOR CHEMOTHERAPY IN BREAST CANCER PATIENTS: A CASE REPORT

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Background/Purpose: Fracture and intravascular embolization of indwelling venous catheter is a rare condition, but it could be a potentially serious complication. Vascular catheters are associated with various complications including infection, thrombosis as well as spontaneous fractures and embolization of the catheter, which is known as 'pinch-off syndrome'.

Methods: A 57-year-old woman with right breast cancer stage I was administrated for 1st FEC (5-fluorouracil, epirubicin, cyclophosphamide) regimen chemotherapy via totally implantable venous access (TIVD) after partial mastectomy. On 2nd chemotherapy, she presented with pain and swelling in left chest when normal saline infused to TIVD. The chest radiograph revealed complete transsection and embolization of the catheter into the inferior vena cava. The embolized TIVD catheter was removed through percutaneous transfemoral retrieval using loop snare without any other complication.

Results: Pinch-off syndrome arises when a subclavian catheter passes through a confined anatomic space and becomes compressed or kinked. With time, repetitive arm motion can lead not only to kinking, but also to perforation and finally fragmentation. It could lead to cardiac or pulmonary complications.

Conclusion: Pinch-off syndrome can easily be prevented by using the external or internal jugular approach. But there is also a certain possibility of transsection or embolization of the catheter, and uncomfortable sensation or pain can be present, especially on neck movement. If no other option is available, it is best to use an axillary approach as opposed to the more traditional medial approach. This ensures that the catheter is within the subclavian vein as it passes through the costoclavicular triangle. Therefore it cannot be compressed.

PO09-12

A RARE CASE OF EXTRAMEDULLARY RELAPSE IN BREAST AFTER COMPLETE REMISSION IN ACUTE MYEROID LEUKEMIA

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Background/Purpose: A 32-year-old woman was referred to the department of breast surgery due to the left breast lump. She had received intensive chemotherapy for acute myeloid leukemia (AML) 7 years ago and achieved a complete remission. The AML was relapsed 4 years ago then allogeneic bone marrow transplantation was performed one year after the relapse. She had been under observation without relapse.

Methods: Six years after initial presentation, a soft tissue mass appeared in the nasal cavity. A biopsy revealed extramedullary relapse of the AML. At the same time, the breast tumor was pointed out.

Results: Ultrasonography showed a hypoechogenic lobular shaped breast tumor in the lower medial quadrant with rough border, the size was 26.5 × 24.3 × 11.3 mm and without invasion of the anterior and the posterior border of the mammary gland. Though the ultrasonographic findings seemed to be a fibroadenoma or a cancer of the breast, extramedurally relapse of the AML could not be ruled out because of her past history. A core needle biopsy showed infiltration of leukemia cells. Although the breast tumor was decreased in size after chemotherapy for AML, the tumor was remained. Bone marrow biopsy showed no leukemia cell in the bone marrow and clinically no relapse was seen except of the left breast. A lumpectomy was performed. Pathological diagnosis for the surgical specimen was invasion of myeloid leukemia in the breast.

Conclusion: A rare case of extramedullary relapse in breast after complete remission of AML is reported.

PO09-13

ACUTE GROWING HUGE BREAST MASS IN POSTMENOPAUSE WOMAN- A CASE REPORT OF INTRACYSTIC PAPILLARY CARCINOMA

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Background/Purpose: Breast carcinoma is the most common cancer in women, the second leading cause of cancer-related mortality in women. Increasing age is a major risk factor for breast cancer incidence and mortality. Invasive papillary carcinoma is rare and comprises less than 1-2% of invasive breast cancers. They are diagnosed predominantly in postmenopausal patients and reported in older age than patients with other types of carcinoma.

Methods: We report a case of intracystic papillary carcinoma of the breast in a 79-year-old woman with acute growing breast mass.

Results: A 79-year-old woman visited our hospital complaining huge breast mass on whole breast. She had first noticed this mass several months ago and since then it abruptly grew and induced pain. On physical examination, she had a palpable, mobile and soft mass. It was nontender, approximately 18 cm and covered whole breast. Mammography showed 18×9 cm sized huge dense mass in left breast and sonography showed 18×8 cm sized huge lobulating heterogeneous hypoechoic mass with echogenic mural nodule with irregular wall thickening. Core-needle biopsy was performed and diagnosis was atypical papilloma. Considering the patient's age and size of mass, we decided to perform a simple mastectomy. The confirmed final diagnosis was intracystic papillary carcinoma with microinvasion. Immunohistochemistry was reported positive for estrogen and progesterone receptors and negative for HER-2 receptor. She received aromatase inhibitor for adjuvant therapy and there was no evidence of recurrence or metastasis on follow-up study.

Conclusion: Intracystic papillary carcinoma should be considered in rapid growing cystic mass of breast on old patients.

PO09-14

CHEMOTHERAPY INDUCED NEUTROPENIC ENTEROCOLITIS WITH ELEVATED MULTIPLE TUMOR MARKERS IN A PATIENT WITH BREAST CANCER

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Background/Purpose: The systemic chemotherapy has improved survival and reduced recurrence for the patients with breast cancer. However, most patients receiving chemotherapy are known to be at risk for adverse side effects, such as bone marrow suppression, cardiotoxicity and gastrointestinal problems.

Methods: We report a case of life-threatening neutropenic enterocolitis with elevated tumor markers associated with chemotherapy in a 59-year-old woman with breast cancer

Results: A 59-year-old woman was diagnosed with invasive ductal carcinoma (T2-N2M0). Neoadjuvant chemotherapy has been arranged with doxorubicin (50 mg/m^2) and docetaxel (75 mg/m^2) every 3 weeks. Two cylces of chemotherapy was tolerated without mild bone marrow suppression and nausea. Approximately 6 days after the administration of 3rd chemotherapy, she began to run a neutropenic fever and 10 days after the administration she had a number of diarrhea and complained with whole abdominal pain. She had abdominal distension and oliguria after 13 days. The computed tomography showed marked low density wall thickening with dilatation of whole colon and large amount of ascites and pleural effusion. CEA (11.72 ng/mL), CA19-9 (95.0 U/mL) and CA-125 (1,708.5 U/mL) were markedly elevated comparing to the results at diagnosis (within normal limit). *Clostridium difficile* toxin was not detected. No malignant cell and reactive change of pleural fluid was showed. She was diagnosed with neutropenic enterocolitis and treated with antibiotics and supportive cares. All the symptoms were improved and tumor markers were within normal range on 20th days since the chemotherapy.

Conclusion: Neutropenic enterocolitis should be considered in patient with chemotherapy and then, tumor markers were possibly elevated.

PO09-15

UPDATED LONGITUDIAL DATA ON ACUTE EXACERBATION OF CHRONIC HEPATITIS B IN PATIENTS WITH BREAST CANCER RECEIVING ANTHRACYCLINE-BASED ADJUVANT CHEMOTHERAPY: THERAPEUTIC VS. PREEMPTIVE USE OF LAMIVUDINE

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Background/Purpose: Following our previous report on acute exacerbation (AE) of chronic hepatitis B (CHB) in breast cancer patients receiving anthracyline-based adjuvant chemotherapy, updated longitudinal data were analyzed focusing on therapeutic and preemptive use of lamivudine.

Methods: Records of 3,259 patients at Asan Medical Center between August 2001 and November 2009 were reviewed. The level of ALT was graded by CTCAE version 3.0. Hepatitis by HBV reactivation was defined as a $\geq$ 10-fold increase in HBV DNA level compared with baseline or an absolute increase of $> 10^5$ copies/mL.

Results: Total 169 patients with positive HBsAg at the start of adjuvant chemotherapy were chosen. Overall, 19 (14.8%) of 128 patients without lamivudine prophylaxis (LP), and 2 (4.9%) of 41 with LP experienced AE of CHB during adjuvant chemotherapy. The old age ($\geq$ 55 years) was only significant predictive factor for AE of CHB ($p = 0.040$) with multivariate analysis.

Conclusion: Preemptive use of lamivudine in patients with breast cancer receiving adjuvant anthracycline-based chemotherapy could reduce the incidence of Grade 3, 4 elevated ALT and hepatitis flare-up. The old age ($\geq$ 55 years) at at the initiation of adjuvant chemotherapy was an independent factor to predict AE of CHB.

Poster Discussion

Table1. Patients characteristics and features of hepatitis

	Lamivudine - *N*=128 (%)	Lamivudine + *N*=41 (%)	*P*
Median age	46	48	NS
Chemotherapy			NS
AC	82 (64.1)	21 (51.2)	
AC+T	46 (35.9)	20 (48.8)	
Median ALT	18	18	NS
Median total bilirubin	0.7	0.8	NS
Level of ALT			0.023
Gr1,2	21 (16.4)	10 (24.4)	
Gr3,4	24 (18.8)	2 (4.9)	
Type of Hepatitis (> 3X ULN)			0.005
HBV related	19 (14.8)	2 (4.9)	0.108 (0.047)*
Non viral , Toxic	23 (18.0)	1 (2.4)	0.010
Onset (after cycle)	4(1-8)	4 (1-8)	NS
Time to resolution (days)	35(5-179)	7 (2-753)	NS
Treatment interruption			NS
>1 wks of delay	20 (15.6)	4 (9.8)	
Discontinuation	12 (9.4)	1 (2.4)	

*if excluding one lamivudine resistant strain (M204V/I, L180M)

Table 1.

PO09-16

AN INVENTORY OF AVON FOUNDATION FOR WOMEN BREAST CANCER PATIENT NAVIGATION PROGRAMS

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Background/Purpose: Avon Foundation for Women grantees provide breast cancer services through patient navigation (PN) in an effort to alleviate barriers among underserved women. To gain a better understanding of how different PN programs function, this study explores variations in the use of navigators, types of services offered, description of clients they serve, tracking of treatment completion, and evaluation mechanisms.

Methods: Using the Avon Foundation for Women database, fifty-six Avon PN programs funded since 2008 throughout the United States were contacted. An online survey was distributed to the grantees of which 44 (81%) complete responses were collected and analyzed.

Results: All programs but 1 offered PN services. Clients were racially and ethnically diverse, mostly in the 40-64 year old age range (64%) and 91.6% with an average income of less than $30,000. Women were either uninsured (50.7%) or receiving Medicaid (32.4%). PN programs were both community and hospital-based (22.5%); most hospitals were described as safety-nets (e.g. provides a significant level of care to low-income, uninsured, vulnerable populations) (35.2%). On-site services included: breast screening (e.g. mammography and breast ultrasound) and treatment (e.g. breast surgery and radiation therapy). Barriers identified to care by the programs included transportation, access to appointments, language barriers, and financial issues (e.g. cost of screening and treatment specifically for those uninsured).

Conclusion: Many Avon PN programs incorporated navigation services that span the cancer care continuum. They addressed disparities by offering navigation and onsite medical services to reduce multiple systems barriers and social issues related to breast care.

PO09-17

MAMMARY FIBROMATOSIS IS MIMICKING CARCINOMA: A CASE REPORT

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Background/Purpose: Mammary fibromatosis is a very rare, benign lesion without metastatic potential and analogous to fibromatosis in other sites. It is characterized by a locally invasive, nonencapsulated, proliferation of well-differentiated spindle cells.

Methods: Clinically, radiologically, it mimics malignancy so only histological analysis confirms the diagnosis. Microscopically, fibromatosis shows rare mitosis and minimal cytologic atypia. Immunohistochemistry is negative for cytokeratins, hormone receptor and positive for vimentin, beta-catenin. The differential diagnosis includes metaplastic carcinoma, spindle cell type low grade fibrosarcoma, nodular fasciitis.

Results: The proper treatment is wide local excision. The major problem is difficulty in defining the border of the tumor intra-operatively because of infiltrativeness of fibromatosis. Recurrence rate is up to 29%. Most of the cases have positive surgical margins and recur within 3 years after surgery. Considering characteristics of mammary fibromatosis, the histopathological differential diagnosis is important for appropriate management. Negative surgical margin is a very important point in treatment. We report a case of huge fibromatosis of breast in a 61-year-old woman.

Conclusion: A 61 years old woman presented a fungated, fetus head size mass with cystic change in her left breast that she had noticed for 1 year. Ultrasonography showed a huge malignant looking mass with necrosis and skin invasion. Core needle biopsy showed findings suggestive of fibromatosis but needed differential diagnosis of metaplastic carcinoma. The result of further incisional biopsy was compatible with fibromatosis. Total mastectomy and skin graft were performed. The definitive were diagnosis of the tumor was fibromatosis with chondrogenesis. The tumor size was 14.6 × 10 cm. All surgical margins were absent of any lesions. The patient was followed up for 1 year without recurrence.

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PU3-2

DISCREPANT RESULTS OF LYMPHOCYTE IN TISS UE AND SERUM IN PATIENTS WITH BREAST CANCER

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Background/Purpose: It is not clear how the systemic response would occur in patients with malignant diseases. There are recent systemic inflammation-based scores, the Glasgow Prognostic Score, Neutrophil Lymphocyte Ratio that have been shown to have prognostic value in cancer patients. The aim of this study is to analyze whether circulatory inflammatory cells such as lymphocytes have relations with characteristics and prognosis of breast cancer.

Methods: We identified 367 patients with histologically proved infiltrating ductal cancer who underwent operation between January 2002 and December 2010. A retrospective multiple medical records including laboratory value (WBC, Neutrophil, Lymphocyte) and histologic results(Histologic grade, nuclear grade, T stage, N stage, ER/PR/c-erbB2 status) was conducted.

Results: Serum WBC, Neutrophil, Lymphocyte count were obtained from total patients. WBC and neutrophil count were do not show signicant correlation, but only the lymphocyte count had significant correlation. In ER positive breast cancer patients, preoperative lymphocyte value (1.90 k/μL) was lower than ER negative group (2.07 k/μL).

Conclusion: In this study we found out that ER-positive patients have lower level of serum lymphocytes. When ER positive patients have better prognosis, this study would not explain results from other studies that show the tumor infiltrating lymphocytes have favorable effects on breast cancer. But it also suggest the host immune response and tumor characteristics are not easily understandable. In conclusion, this study could explain the dormant characteristics of ER positive breast cancer and needs further study about the immune response against breast cancer.

Publication Only

PU4-1

THE EFFECT OF THE HYPERTHERMIA THERAPY COMBINED WITH CHEMOTHERAPY AND/OR HORMONAL THERAPY ON LIVER METASTASIS OF BREAST CANCER

Rika Fukui[1], Takahiro Yasoshima[1], Hideyuki Morosawa[2], Yoshihiko Furuta[2], Sadahisa Tokuda[3]

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[3]*Department of Neurosurgery, Teishinkai Hospital, Japan*

Background/Purpose: Liver metastasis is one of the life-threatening factors for the breast cancer patients.

Methods: In our institute, we performed weekly hyperthermia therapy combined with chemotherapy and/or hormonal therapy for 9 patients who have liver metastasis of breast cancer.

Results: The duration of the therapy ranges 3 to 23 months and no severe adverse effects have occurred. Among them, 5 patients achieved 3 months or more progression free survival time (median 7 months). Survival time from liver metastasis ranges 13 to 40 months (median 24 months).

Conclusion: Hyperthermia therapy for liver metastasis of breast cancer could have additive effect on chemotherapy and hormonal therapy. Furthermore, hyperthermia therapy is tolerable and it could be performed for the patients on the end stage of the disease.

PU4-2

THE EFFECT AND BENEFIT OF HYPERTHERMIA THERAPY COMBINED WITH LOW DOSE CHEMOTHERAPY AND/OR HORMONAL THERAPY FOR ADVANCED BREAST CANCER PATIENTS

Hideyuki Morosawa[1], Yoshihiko Furuta[1], Yoshiki Miya[1], Rika Fukui[2], Takahiro Yasoshima[2], Sadahisa Tokuda[3]

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Background/Purpose: Although there are a number of anticancer drugs and hormonal agents for the treatment of breast cancer, the effect of them is limited.

Methods: In our institute, we performed weekly hyperthermia therapy combined with low dose chemotherapy and/or hormonal therapy for 23 cases of stage IV or metastatic breast cancer.

Results: The duration of the therapy ranges 6 to 33 months and no severe adverse effects has occurred. Among them, 13 patients achieved 3 months or more progression free survival time (median 7 months). They started hyperthermia therapy earlier than the other patients; their average number of metastatic organ on the start of hyperthermia therapy is 1.53, compared to the other's 2.20.

Conclusion: Further experience and follow up of the patients will demonstrate this treatment is effective and supportive for patients' quality of life.

Publication Only

PU4-3

THE IMPACT OF OBESITY ON RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN OPERABLE BREAST CANCER PATIENTS

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Background/Purpose: The association between obesity and response to neoadjuvant chemotherapy in breast cancer patients is not clear. We evaluated the impact of obesity on response to neoadjuvant chemotherapy in patients with operable breast cancer.

Methods: From May 2000 to December 2010, 104 patients were diagnosed with invasive breast cancer at Korea University Anam Hospital and received neoadjuvant chemotherapy before surgery. Patients were classified into those of normal (BMI of 18.5 to < 25 kg/m^2), overweight (BMI of 25 to < 30 kg/m^2), or Obese (BMI ≥ 30 kg/m^2). The association between body mass index and pathologic response [pathologic complete response (pCR) and pathologic partial response (pPR)] to neoadjuvant chemotherapy was examined using logistic regression.

Results: Median age was 45 years. Mean BMI was 24.8 kg/m^2; 53.8% had a normal BMI, 35.6% overweight, and 10.6% of patients was obese. BMI did not show a significant association with estrogen receptor (ER) status, progesterone receptor (PR) status, HER-2 status, lymph node involvement and neoadjuvant chemotherapy regimen. In univariate analysis, obese patients were significantly less likely to have a pCR and pPR compared with normal weight patients (odds ratio [OR] = 0.317; 95% CI, 0.123-0.821; p = 0.018). In multivariate analysis, ER negativity was significantly associated with a pCR and pPR to neoadjuvant chemotherapy (OR = 5.323; 95% CI, 1.115-25.412; p = 0.036), but there was no significant difference in pCR and pPR for obese patients compared with normal weight patients (OR = 0.508;95% CI, 0.174-1.483; p = 0.215).

Conclusion: Our study suggests that obesity should be considered to be a factor of worse response to neoadjuvant chemotherapy in patients with operable breast cancer.

PU4-4

LEARNING CURVE FOR EXCISION OR BIOPSY OF BREAST LESIONS USING ULTRASOUND-GUIDED VACUUM ASSISTED BREAST BIOPSY SYSTEM

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Background/Purpose: Excision using ultrasound-guided vacuum assisted breast biopsy system (VABB) is a well accepted alternative modality to diagnose and treat a benign breast mass. The purpose of the study is to evaluate a learning curve for ultrasound-guided VABB excision.

Methods: Total 54 patients who underwent ultrasound-guided VABB excision or biopsy consecutively from April to August 2008 were analyzed. To identify factors related to learning periods, we divided patients into 2 groups; the first 20 consecutive patients as group A and the late 34 consecutive patients as group B.

Results: Fifty-two patients received excision, and two underwent biopsy only. Five- and 10-day moving averages curves showed that there was a plateau phase after performing VABB procedures after the 20th patient. VABB probe position significantly influence on total operation time ($p = 0.01$). Total operation time of the first excised or biopsied lesions of group B were significantly much shorter than that of group A ($p < 0.001$). The incidence of bruise or hematoma tended to be less frequently observed in group B than in group A, and VABB probe position of group B during procedure tended to be better than that of group A, however, those were not statistically significant. There was no case of re-operation for delayed bleeding.

Conclusion: It is suggested that the learning curve for ultrasound-guided VABB may exist and VABB procedures may be an easy performing and relatively safe modality for diagnosis and treatment of benign breast lesions.

Publication Only

PU5-2

HOW TO EVALUATE THE BREAST ASYMMETRY WITHOUT MICROCALCIFICATION ON SCREENING MAMMOGRAPHY IN KOREAN WOMEN?

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Background/Purpose: The purpose of this study was to evaluate the effectiveness of diagnostic mammography and/or targeted Ultrasonography (US) for the evaluation of the breast asymmetry without microcalcification on screening mammography in Korean women

Methods: A database search from January 2006 to December 2007 was performed to find patients who performed additional mammography of spot compression view and targeted ultrasound for further evaluation of asymmetry without microcalcifications. A total of 252 asymmetries on mammography were noted. Findings of routine screening mammography, US, and additional mammography were retrospectively reviewed and compared with the biopsy results of fellow-up data.

Results: Of 252 screening mammography detected asymmetry without microcalcifications, 109 (43.3%) patients have fatty breast whereas 143 (56.7%) have dense breast. Four lesions were confirmed as malignancy. Imaging findings of 104 lesions (41.3%) were negative on both targeted US and additional mammographic views. Abnormal findings only on additional mammographic view were noted in 52 lesions, only on US in 28 lesions, whereas 48 lesions showed abnormal findings on both exams. Among 20 lesions were classified as category 4, two of them finally revealed as invasive ductal carcinoma and other two as ductal carcinoma *in situ*. These four cancers also showed suspicious findings on both US and additional mammographic views. All malignancy was identified in cases with developing asymmetry on routine mammography.

Conclusion: In cases of screen mammography detected asymmetry without microcalcifications, diagnostic mammographic view is acceptable first line study for further evaluation in Korean women.

PU5-3

EVALUATION OF AXILLARY SONOGRAPHY AS A PREOPERATIVE DIAGNOSTIC METHOD

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Background/Purpose: Axillary Ultrasound (US) is a useful method in assesing the status of axillary lymph nodes. So we planned to evaluate the diagnostic accuracy of axillary US and/or fine needle aspiration cytoloby (FNAC) performed by surgeons in determining axillary nodal status preoperatively.

Methods: High-resolution sonography was used for pre-op evaluation in 38 patients with unknown nodal status who underwent axillary lymph node dissection. Axillary US was performed by 5 breast surgeons experienced in ultrasound and biopsy techniques. US guided FNAC was used to evaluate suspicious nodes Axillary US and FNAC results were compared with final axillary histology.

Results: 10 patients had axillary nodal metastasis. 12 cases had T2 stages. The positive predictive value and negative predictive value were 100% and 82%, respectively. Specificity in all axillary lymph node metastasis cases was 60%. Specificity in T2 stage cases is 80%.

Conclusion: Preoperative ultrasound (US) combined with FNAC has been proved to be the most reliable method to detect nonpalpable axillary metastases in patients with breast cancer. We concluded that routine preoperative axillary sonography with or without FNAC seems to be one of methods to be complementary to sentinel node biopsy and reduce unnecessary axillary procedures.

Publication Only

PU7-1

CLINICOPATHOLOGIC FACTORS THAT PREDICT RESPONSES TO TRASTUZUMAB IN HER2-OVEREPRESSED BREAST CANCER

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Background/Purpose: Trastuzumab, a humanized antibody against HER2 protein, is widely used as a standard therapeutic agent for patients with HER2-overexpressed breast cancer. Although it shows high activity to improve the prognosis of many patients treated, not all patients with HER2-overexpressed cancer benefit from the regimen. The aim of this study was to identify clinicopathologic factors in patients with breast cancer that predict responses to trastuzumab-containing regimens.

Methods: Twenty-one patients with locally advanced or metastatic breast cancer showing HER2 overexpression were treated with trastuzumab-containing regimens from April 2004 to December 2010. Clinicopathologic factors such as age, number of involved organ sites, cytotoxic drugs administered in combination with trastuzumab, serum tumor marker levels, hormonal status and positivity of HER2-overexpressed cancer cells were compared in 14 responders and 7 non-responders to the treatment.

Results: The percentage of cancer cells positive for HER2 in the tumor was significantly higher in the responders than in the non-responders. Serum level of HER2 extracellular domain (ECD), but not serum levels of other tumor markers, was significantly higher in the responders than in the non-responders. Age, cytotoxic drugs used, hormonal status and number of involved organ sites showed no association with the response.

Conclusion: Positivity of HER2 in the tumor and serum HER2 ECD level can be useful for predicting responses to treatment with trastuzumab in patients with HER2-overexpressed breast cancer.

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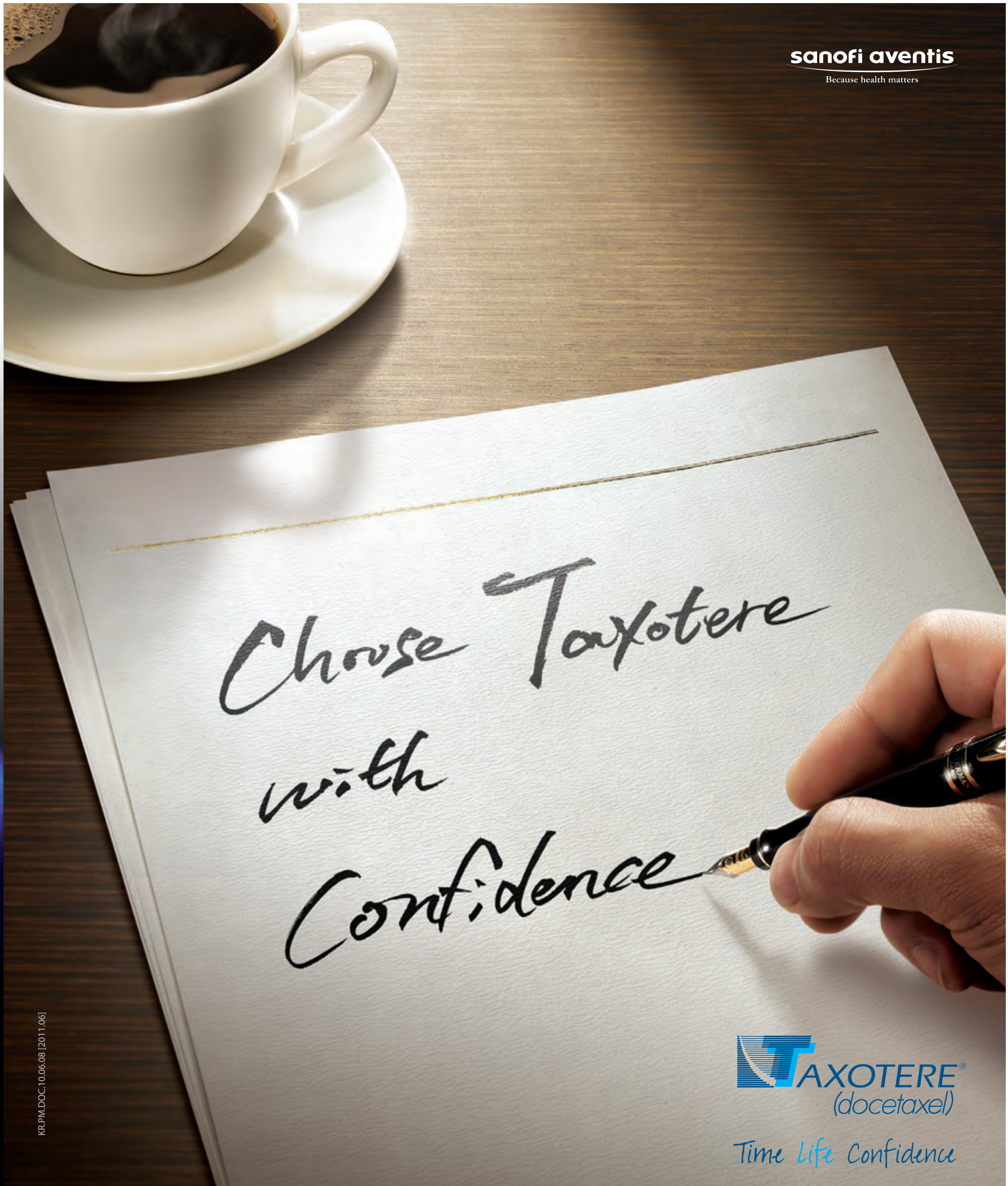

탁소텔주 (도세탁셀삼수화물)

전문의약품

〈원료약품 및 그 분량〉 이 약 본액 1ml중 주성분 도세탁셀삼수화물(별규) 42.68mg (도세탁셀무수화물로서 40.0mg) **〈효능효과〉** **• 유방암 :** 독소루비신과 병용하여 국소적으로 진행된 또는 전이된 유방암의 1차 치료, HER2(Human Epidermal growth factor Receptor 2 protein)가 과발현(IHC 3+ 또는 FISH 양성)되고 화학요법 치료를 받은 경험이 없는 전이성 유방암에 트라스투주맙과 병용요법제로 사용, 이전의 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암, 카페시타빈과 병용하여 Anthracycline계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암의 치료, 독소루비신과 시클로포스파미드와 병용하여 수술가능한 림프절 양성 유방암의 수술 후 보조요법 **• 비소세포 폐암:** 백금화학요법제로 치료효과를 얻지 못한 환자들을 포함한 국소적으로 진행된 비소세포폐암 또는 전이성 비소세포폐암 **• 전립선암 :** 프레드니솔론과 병용하여 안드로겐 비의존성(호르몬불응성) 전이성 전립선암의 치료 **• 난소암 :** 카보플라틴과 병용하는 1차요법제로서 진행된 또는 전이된 상피성 난소암 **• 두 · 경부암:** 시스플라틴 및 5–플루오로우라실과 병용하여 국소 진행성 두경부 편평세포암의 유도화학요법 **• 위암:** 진행성 및 전이성 또는 국소재발성 위암의 단독요법, 시스플라틴 및 5–플루오로우라실과 병용하여 전이성 또는 국소재발성 위암의 1차 치료 **• 식도암:** 진행성 또는 재발성 식도 편평세포암 **〈용법용량〉** **• 유방암:** 유방암에 대한 일차적 요법에서 독소루비신(50mg/m^2)과 병용시 도세탁셀 75mg/m^{2}을 투여한다. –화학요법 치료를 받은 적이 없는 HER2 과발현 전이성 유방암에 트라스투주맙과 병용요법제로 사용하는 경우, 도세탁셀 100mg/m^2 를 매 3주마다 60분에 걸쳐 점적정주한다. 트라스투주맙 첫 투여 다음날 도세탁셀 투여를 시작할 수 있고, 이전 투여한 라스투주맙의 내약성이 좋았다면 트라스투주맙 투여 직후 도세탁셀 투여를 시작할 수도 있다. *트라스투주맙은 초기용량으로 체중 kg 당 4mg을 90분에 걸쳐 점적 정주한 후 다음 주부터는 매주 체중 kg 당 2mg을 투여한다. (트라스투주맙 제품의 용법,용량 참조) – 이전 화학요법에 실패한 유방암에서는 도세탁셀 75~100mg/m^{2}을 매 3주마다 1시간 동안 정맥 투여한다. – 카페시타빈과 병용하여 Anthracycline계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암에서는 3주마다 도세탁셀을 75mg/m^2 투여하면서 카페시타빈을 2주간 1일 2회, 1회 1,250mg/m^2 투여하고(식후 30분 이내) 1주간 휴약하는 것(3주를 주기로 함)이 권장된다. 카페시타빈 용량은 카페시타빈의 제품설명서를 참조하여 체표면적에 따라 결정한다. – 독소루비신과 시클로포스파미드와 병용하여 림프절양성, 수술가능한 유방암환자에서 수술후 보조요법으로 매 3주마다 독소루비신과 시클로포스파미드 투여 1시간 후 도세탁셀 75mg/m^{2}를 6주기 투여한다. 혈액학적 독성 위험을 줄이기 위해서는 예방적으로 G–CSF를 투여할 수 있다 (용량조절항 참조) **• 비소세포 폐암:** 도세탁셀 75~100mg/m^{2}을 매 3주마다 1시간동안 정맥주사한다. 백금 유도체와 복합화학요법으로 치료시 최대 75mg/m^{2}으로 정맥 투여한다. **• 전립선암:** 프레드니솔론과 병용시 도세탁셀 75mg/m^{2}을 매 3주마다 1시간 동안 정맥주사한다. 프레드니솔론은 1일 2회, 1회 5mg을 지속적으로 경구투여한다. **• 난소암:** 진행된 또는 전이된 상피성 난소암에 대한 일차적 요법으로는 카보플라틴과 병용하여 3주마다 도세탁셀 75mg/m^2 1시간동안 정맥주사 후 즉시 카보플라틴 AUC 6.0mg/ml.min을 30~60분간 정맥주사한다. **• 두 · 경부암:** 방사선요법 전의 유도화학요법: 75mg/m^2 을 1시간동안 정맥주사한 후, 시스플라틴 75mg/m^2 을 1시간 이상 정맥주사한다 (제 1일). 그 후 5–플루오로우라실을 750mg/m^2/day로 5일동안 연속 정맥주사한다. 3주를 1주기로 하여 4주기 동안 투여한다. 화학요법을 받은 후 방사선 요법을 받도록 한다.–화학방사선요법 전의 유도화학요법: 75mg/m^2 을 1시간동안 정맥주사한 후, 시스플라틴 100mg/m^2 을 30분–3시간 동안 정맥주사한다. (제 1 일). 그 후 5–플루오로우라실을 1,000mg/m^2/day로 연속 정맥주사한다 (제1–4일). 3주를 1주기로 하여 3주기 동안 투여한다. 화학요법을 받은 후 화학방사선 요법을 받도록 한다. **• 위암:** 단독요법: 75mg/m^2 매 3주마다 1시간동안 정맥 주사한다. 시스플라틴 및 5–플루오로우라실과 병용투여: 75mg/m^2 을 1시간 동안 정맥주사 후, 시스플라틴 75mg/m^2 을 1–3시간 동안 정맥주사한다. 시스플라틴 정맥주사가 끝난 후부터 5–플루오로우라실을 750mg/m^2/일 용량으로 5일동안 연속주입한다 (1주기). 3주마다 같은 방법으로 투여한다. **• 식도암:** 상용량은 성인에게 1일 1회 도세탁셀 70mg/m^{2}을 1시간 이상 3~4주 간격으로 정맥 주사하며, 환자의 상태에 따라 적절히 감량한다. **〈금기〉** 1) 이 약 및 폴리소르베이트 80에 대해 과민반응의 병력이 있는 환자 2) 호중구수가 1,500/mm^3 이하인 환자 3) 임부 및 수유부 4) 중증 간기능장애 환자 5) 병용투여시, 병용약물에 금기인 환자(중증 신기능장애 환자, 파라플라틴, 백금화합물, 만니톨에 과민한 환자 등) 6) 감염증의 합병증이 있는 환자 7) 감염성 발열이 의심되는 환자 8) 중증의 골수 억제가 있는 환자 **〈신중투여〉** 1) 골수억제가 있는 환자 2) 간기능장애 환자 3) 신기능장애 환자 4) 간질성 폐렴 또는 폐섬유증이 있는 환자 5) 부종이 있는 환자 6) 임신할 가능성이 있는 환자. 기타 이상반응은 제품의 사용설명서 참조. ※ 보다 상세한 제품정보는 제품설명서를 참조하시기 바랍니다. **수입판매자:** (주)사노피–아벤티스 코리아 **제조의뢰자 :** Aventis Pharma S.A., France **제조자 :** Aventis Pharma Dagenham, UK, (주)사노피–아벤티스 코리아 서울 강남구 역삼1동 735번지 T.02–527–5500 F.02–527–5551 www.sanofi–aventis.co.kr

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Aromatase Inhibitor mythology

유방암 치료제의 신화 페마라가 만듭니다.

페마라는 조기 보조요법으로 사용시 원격전이의 위험을 타목시펜 대비 유의하게 낮춘 아로마타아제 억제제 입니다.[1-4]

BIG-1-98 study
26개월 추적 조사 결과,

19% 19% 재발위험 감소 (P=0.003)[2]

27% 27% 원격전이의 위험 감소 (P=0.001)[2]

51개월 추적 조사 결과,

18% 18% 재발위험 감소 (P=0.007)[3]

19% 19% 원격전이의 위험 감소 (P=0.03)[3]

Because breast cancer doesn't stop at the breast.

페마라® 레트로졸

Ref.) 1. FEMARA [summary of product characteristics]. Basel. Switzerland: Novartis Pharma AG:2006 2. Thurlimann B. for the BIG 1-98 Collaborative Group. A Comparison of Letrozole and Tamoxifen in Postmenopausal Women with Early Breast Cancer. N Engl J Med. 2005;353:2747-57 3. Alan S. Coates et al. Five Years of Letrozle Compared with Tamoxifen As Initial Adjuvant Therapy for Postmenupausal Women With Endocrine-Responsive Early Breast Cancer: Update of Study BIG 1-98. J clin Oncol. 2007;25:486-492 4. Gradishar W. Landmark Trials in Endocrine Adjuvant Therapy for Breast Carcinoma. Cancer. 2006;106:975-981.

페마라® 정(레트로졸) • **주성분:** 레트로졸 2.5mg • **적응증:** · 에스트로겐 또는 프로게스테론 수용체 양성이거나 수용체 상태가 알려지지 않은 폐경후 여성의 국소적으로 진전된 또는 전이성 유방암에서 1차 치료 · 항 에스트로겐 요법 후 재발된 자연적 또는 인공적으로 폐경이 된 여성의 진전된 유방암 · 에스트로겐 또는 프로게스테론 수용체 양성이거나 수용체 상태가 알려지지 않은 폐경후 여성의 조기 유방암에서 5년동안 타목시펜 보조요법이후 연장 보조 용법 · 호르몬수용체 양성인 폐경후 여성의 조기 유방암에서의 보조요법 • **용법용량:** 1일 1회 2.5mg 복용 **금기:** 이 약의 주성분이나 부형제에 과민증환자, 폐경 전 내분비 상태인 여성, 임부, 수유부 • **신중투여, 주의:** 크레아티닌 클리어런스가 10mL/min미만인 환자는 이 약 치료의 잠재적 유익성 및 위험성을 신중히 고려해야 한다. 심한 간부전 환자(Child-Pugh score C)는 세심한 관찰 하에 투여되어야 한다. • **이상반응:** 가장 흔한 이상반응은 안면홍조, 오심, 피로, 관절통이며, 흔한 부작용은 식욕부진,식욕증가, 말초부종, 두통, 어지러움, 구토, 소화불량, 변비, 설사, 탈모증, 발한 증가, 발진, 근육통, 뼈의 통증, 관절염, 골절, 골다공증, 체중증가, 고콜레스테롤혈증, 우울증이다. 드물게 발생하나 심각할 가능성이 있는 부작용은 백혈구감소증, 백내장, 뇌혈관 사고 또는 경색, 혈전정맥염, 폐색전, 동맥혈전증, 허혈성심혈관질환이다. ※ 처방하시기 전, 상세 제품정보를 참조하시기 바랍니다.

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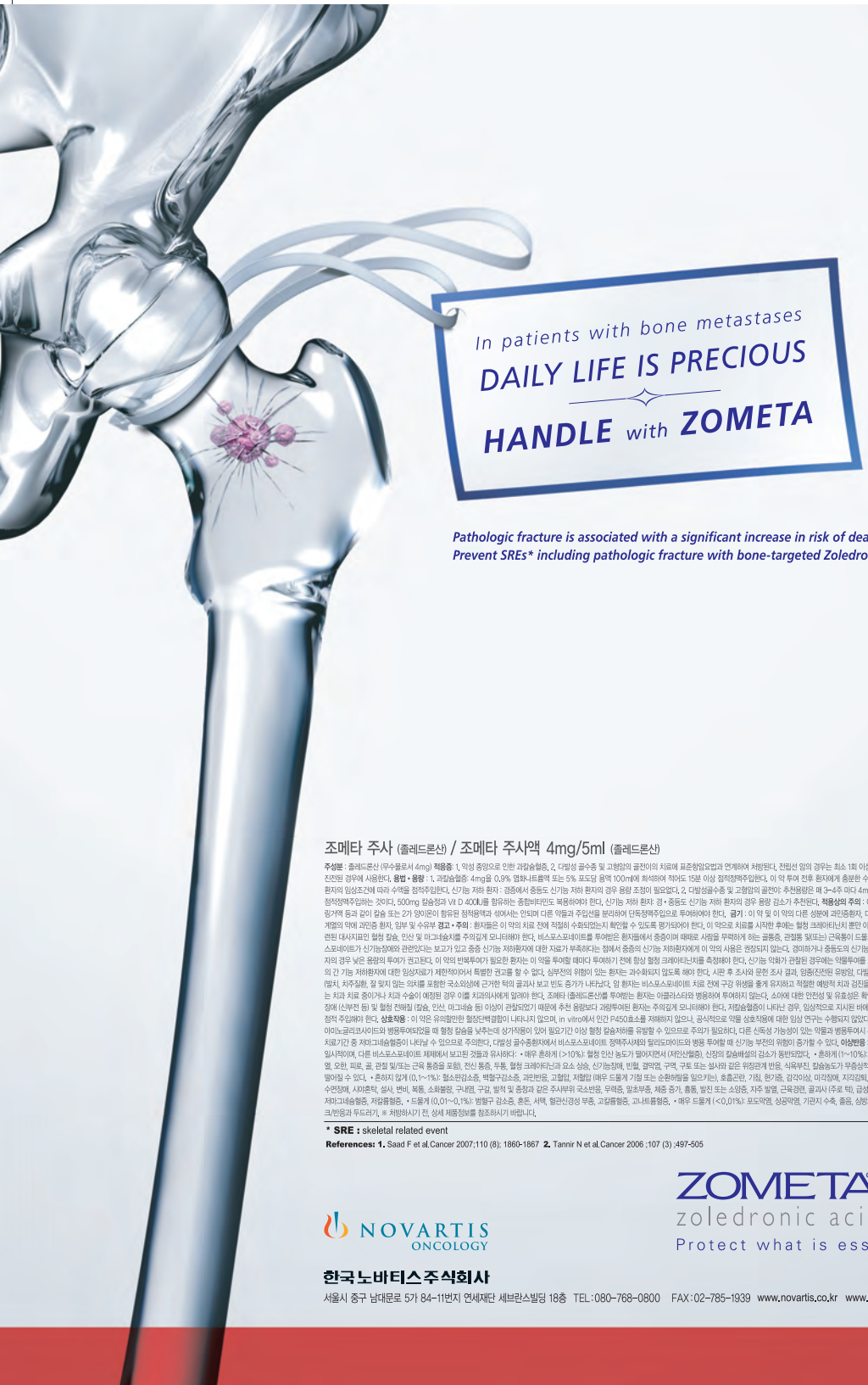

Pathologic fracture is associated with a significant increase in risk of death.
Prevent SREs including pathologic fracture with bone-targeted Zoledronic acid.*[1,2]

조메타 주사 (졸레드론산) / 조메타 주사액 4mg/5ml (졸레드론산)

주성분 : 졸레드론산 (무수물로서 4mg) **적응증** : 1. 악성 종양으로 인한 과칼슘혈증, 2. 다발성 골수종 및 고형암의 골전이의 치료에 표준항암요법과 연계하여 처방된다. 전립선 암의 경우는 최소 1회 이상 호르몬 치료 후 병이 진전된 경우에 사용한다. **용법 • 용량** : 1. 과칼슘혈증: 4mg을 0.9% 염화나트륨액 또는 5% 포도당 용액 100ml에 희석하여 적어도 15분 이상 점적정맥주입한다. 이 약 투여 전후 환자에게 충분한 수분이 공급되도록 하고 환자의 임상조건에 따라 수액을 점적주입한다. 신기능 저하 환자 : 경증에서 중등도 신기능 저하 환자의 경우 용량 조정이 필요없다. 2. 다발성골수종 및 고형암의 골전이: 추천용량은 매 3~4주 마다 4mg을 적어도 15분 이상 점적정맥주입하는 것이다, 500mg 칼슘정과 Vit D 400IU를 함유하는 종합비타민도 복용하여야 한다. 신기능 저하 환자: 경 • 중등도 신기능 저하 환자의 경우 용량 감소가 추천된다. **적용상의 주의** : 이 약은 락트산을 기한 링거액 등과 같이 칼슘 또는 2가 양이온이 함유된 점적용액과 섞어서는 안되며 다른 약들과 주입선을 공리하여 단독정맥주입으로 투여하여야 한다. **금기** : 이 약 및 이 약의 다른 성분에 과민증환자, 다른 비스포스포네이트 계열의 약제 과민증 환자, 임부 및 수유부 **경고 • 주의** : 환자들은 이 약의 치료 전에 적절히 수화되었는지 확인할 수 있도록 평가되어야 한다. 이 약으로 치료를 시작한 후에는 혈청 크레아티닌치 뿐만 아니라 과칼슘혈증과 관련된 대사지표인 혈청 칼슘, 인산 및 마그네슘농도를 주의깊게 모니터해야 한다, 비스포스포네이트를 투여받은 환자들에서 중증이며 때때로 사망을 부력하게 하는 골괴증, 관절통 및(또는) 근육통이 드물게 보고되었다, 비스포스포네이트나 신기능장애와 관련있다는 보고가 있고 중증 신기능 저하환자에 대한 자료가 부족하다는 점에서 중증의 신기능 저하환자에게 이 약의 사용은 권장되지 않는다. 경미하거나 중등도의 신기능부전을 가진 골전이환자의 경우 낮은 용량의 투여가 권고된다. 이 약의 반복투여가 필요한 환자는 이 약을 투여할 때마다 투여하기 전에 혈청 크레아티닌치를 측정해야 한다, 신기능 악화가 관찰된 경우에는 약물투여를 보류하여야 한다, 중증의 간 기능 저하환자에 대한 임상자료가 제한적이며서 특별한 권고를 할 수 없다, 심부전의 위험이 있는 환자는 과수화되지 않도록 해야 한다, 시판 후 조사와 문헌 조사 결과, 암중간전염 유방암, 다발성골수종과 저하상태 (발치, 치주질환, 잘 맞지 않는 의치를 포함한 국소외상)에 근거한 턱의 골괴사 보고 빈도 증가가 나타났다, 암 환자는 비스포스포네이트 치료 전에 구강 위생을 좋게 유지하고 적절한 예방적 치과 검진을 받아야 한다, 암 환자는 치과 치료 중이거나 치과 수술이 예정된 경우 이를 치과의사에게 알려야 한다, 조메타 (졸레드론산)를 투여받는 환자는 아클라스타와 병용하여 투여하지 않는다, 소아에 대한 안전성 및 유효성은 확립되지 않았다, 신기능장애 (신부전 등) 및 혈청 전해질 (칼슘, 인산, 마그네슘 등) 이상이 관찰되었기 때문에 추천 용량보다 과량투여된 환자는 주의깊게 모니터해야 한다, 저칼슘혈증이 나타난 경우, 임상적으로 지시된 바에 따라 글루콘산칼슘을 정적 주입해야 한다, **상호작용** : 이 약은 유의함만한 혈장단백결합이 나타나지 않으며, in vitro에서 인간 P450효소를 저해하지 않으니, 공식적으로 약물 상호작용에 대한 임상 연구는 수행되지 않았다, 비스포스포네이트는 이미노글리코사이드와 병용투여되었을 때 혈청 칼슘을 낮추는데 상가작용이 있어 필요기간 이상 혈청 칼슘저하를 유발할 수 있으므로 주의가 필요하다, 다른 신독성 가능성이 있는 약물과 병용투여시 주의가 필요하다, 또한 치료기간 중 제마그네슘혈증이 나타날 수 있으므로 주의한다, 다발성 골수종환자에서 비스포스포네이트 정맥주사제와 탈리도마이드와 병용 투여할 때 신기능 부전의 위험이 증가할 수 있다, **이상반응** : 일반적으로 경증이고 일시적이며, 다른 비스포스포네이트 제제에서 보고된 것들과 유사하다: • 매우 흔하게 (>10%): 혈청 인산 농도가 떨어지면서 (저인산혈증), 신장의 칼슘배설의 감소가 동반되었고, • 흔하게 (1~10%): 인플루엔자양 증상발열, 오한, 피로, 골, 관절 및/또는 근육 통증을 포함, 전신 통증, 두통, 혈청 크레아티닌과 요소 상승, 신기능장애, 빈혈, 결막염, 구역, 구토 또는 설사와 같은 위장관계 반응, 식욕부진 칼슘농도가 무증상적 저칼슘혈증 수준으로 떨어질 수 있다, • 흔하지 않게 (0,1~1%): 혈소판감소증, 백혈구감소증, 과민반응, 고혈압, 저혈압 (매우 드물게 기절 또는 순환허탈을 일으키는), 호흡곤란, 기침, 현기증, 감각이상, 미각장애, 지각감퇴, 감각과민, 진전, 불안, 수면장애, 시야흐릿, 설사, 변비, 복통, 소화불량, 구내염, 구갈, 발적 및 종창과 같은 주사부위 국소반응, 무력증, 말초부종, 체중 증가, 흥통, 발진 또는 소양증, 자주 발열, 근육경련, 골괴사 (주로 턱), 급성 신부전, 혈뇨, 단백뇨, 제마그네슘혈증, 저칼륨혈증, • 드물게 (0,01~0,1%): 범혈구 감소증, 혼돈, 서맥, 혈관신경성 부종, 고칼륨혈증, 고나트륨혈증, • 매우 드물게 (<0,01%): 포도막염, 상공막염, 기관지 수축, 홍음, 상방세동, 아나필락시스 쇼크/반응과 두드러기, ※ 처방하시기 전, 상세 제품정보를 참조하시기 바랍니다.

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* **SRE :** skeletal related event

References: 1. Saad F et al.Cancer 2007;110 (8): 1860-1867 **2.** Tannir N et al.Cancer 2006 ;107 (3) :497-505

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