



Global
Breast Cancer
Conference
2007

New Horizon & Hope for Cure

A B S T R A C T B O O K

Global Breast Cancer Conference 2007

October 11~13, 2007 Sheraton Grande Walkerhill Seoul, Korea

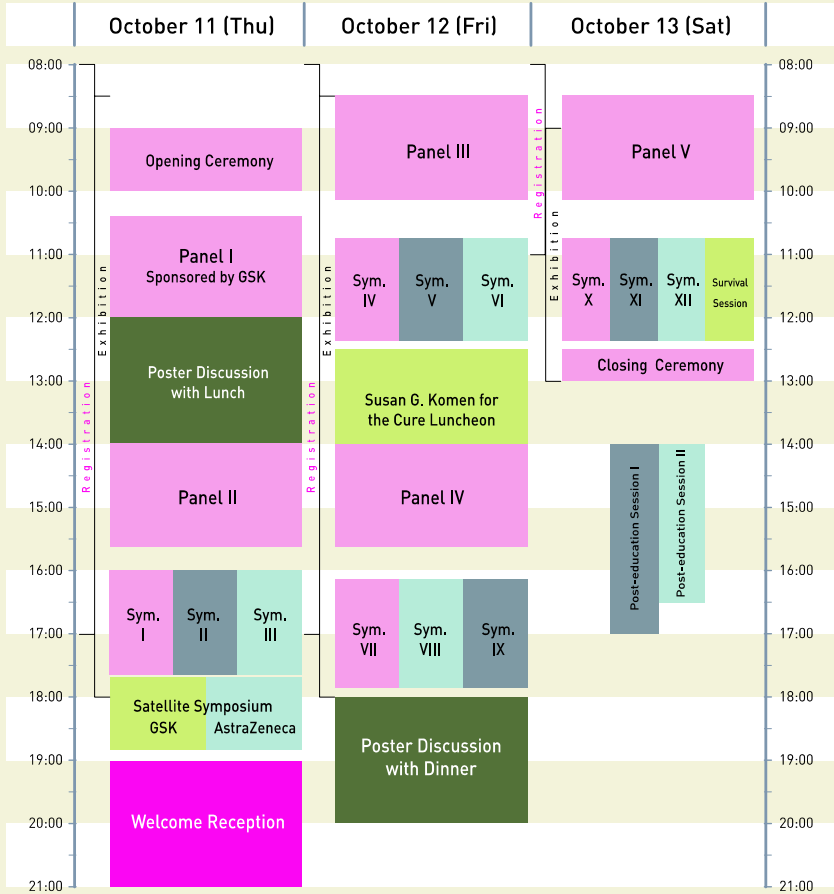
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PROGRAM AT A GLANCE





 Vista Hall (B2)

 Vista Hall I & II (B2)

 Vista Hall III (B2)

 Grand Hall I (B1)

 Grand Hall II & III (B1)

 Mugunghwa Hall (1F)

SCIENTIFIC PROGRAM

Opening Ceremony

09:00-10:00 / October 11, 2007

Vista Hall I+II

Panel I: Breast Cancer in Asian and Western Countries; Is it a Different Disease?

10:20-12:00 / October 11, 2007

Vista Hall I+II

Moderator: Hy-De Lee Yonsei University Yongdong Severance Hospital, Korea

- P1-1 Clinical Characteristics and Survival Analysis of Korean Breast Cancer Patients** — 3
Eil-Sung Chang
Chungnam National University Hospital, Korea
- P1-2 Breast Cancer as a Public Health Problem** — 4
Hee-Soon Juon
Johns Hopkins Bloomberg School of Public Health, USA
- P1-3 Is it Breast Cancer a Different Disease in Asian Women?** — 5
Jorge Otero¹, Hanlim Moon², Christine Perry³, Annette Gross³
¹International Medical Oncology Philadelphia, USA, ²Asia Pacific Clinical Development Oncology Singapore,
³Ethnopharmacology Australia, Singapore, USA GlaxoSmithKline Research & Development

Lunch with Poster Discussion

12:00-14:00 / October 11, 2007

Grand Hall I

Panel II: Prevention of Breast Cancer

14:00-15:40 / October 11, 2007

Vista Hall I+II

Moderator: Sara Sukumar The Kimmel Cancer Center at Johns Hopkins, USA

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Junichi Kurebayashi
Department of Breast and Thyroid Surgery, Kawasaki Medical School, Japan
- P2-2 Preventive Choices for High Risk Women Based on Gene-Environment Interaction of Breast Cancer** — 7
Daehee Kang
Department of Preventive Medicine, Seoul National University College of Medicine, Korea
- P2-3 Novel and Intraductal Approaches to Chemoprevention of Breast Cancer** — 9
Sara Sukumar¹, Vered Stearns¹, Tsuyoshi Mori¹, Nagi Khouri¹, Susan Love², Theodore Tsangaris¹
¹Department of Oncology, Johns Hopkins University, School of Medicine, USA, ²Windy Hill Medical, USA
- P2-4 Promotion of Mammography: What Can Be Learned from the U.S. Experience?** — 10
Helen Meissner
Applied Cancer Screening Research Branch, Division of Cancer Control and Population Sciences,
National Cancer Institute, USA

Symposium I: Current Issues for Breast Cancer Treatment I

16:00-17:40 / October 11, 2007

Vista Hall I+II

Moderators: **Louis Chow** Organization for Oncology and Translational Research Ltd, Hong Kong
HeeSook Park Soonchunhyang University Hospital, Korea

- S1-1 Strategies for the Use of Adjuvant Aromatase Inhibitors** ————— 25
Walter Jonat
University Hospital Schleswig-Holstein, Germany
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Woo Chul Noh
Department of Surgery, Korea Cancer Center Hospital, Korea
- S1-3 Neoadjuvant Hormonal Therapy for Breast Cancer** ————— 28
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Organization for Oncology and Translational Research Ltd, Hong Kong
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Sun Young Rha
Department of Internal Medicine, Yonsei University College of Medicine, Korea

Symposium II: Prediction, Screening, Early Detection

16:00-17:40 / October 11, 2007

Vista Hall III

Moderators: **Norma Kanarek** Johns Hopkins Bloomberg School of Public Health, USA
Pa Jong Jung Jung Pa Jong Clinic, Korea

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Department of Preventive Medicine, Seoul National University College of Medicine, Korea
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Department of Surgery and Breast Surgery, Cancer Hospital, Fudan University, China
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National Cancer Center, Korea
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L Erby, D Roter
Department of Health, Behavior and Society; The Johns Hopkins Bloomberg School of Public Health, USA

Symposium III: Cancer Surveillance and Education

16:00-17:40 / October 11, 2007

Grand Hall II+III

Moderators: Ann Klassen Johns Hopkins Bloomberg School of Public Health, USA
Sei-Hyun Ahn Asan Medical Center, Korea

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Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, USA
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Department of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, USA

Satellite Symposium (Organized by GSK)

17:40-18:50 / October 11, 2007

Mugunghwa Grand Ballroom

Korea-Japan Advisory Meeting (Organized by AstraZeneca)

17:40-18:50 / October 11, 2007

Grand Hall II+III

Panel III: Breaking News in Breast Cancer Treatment

08:30-10:10 / October 12, 2007

Vista Hall I+II

Moderator: Koing Bo Kwun Keimyung University Dongsan Medical Center, Korea

- P3-1 Surgical Treatment: Controversies and Challenges in Surgical Treatment for Early Breast Cancer** ————— 11
Min-Hyuk Lee
Department of Surgery, College of Medicine, Soonchunhyang University, Korea
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Soonmyung Paik
Division of Pathology, NSABP Foundation, USA
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Jo Anne Zujewski
National Cancer Institute, USA

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10:40-12:20 / October 12, 2007

Vista Hall I+II

Moderators: Shin-Cheh Chen Chang Gung Memorial Hospital, Taiwan

Jung Sil Ro National Cancer Center, Korea

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Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea
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Seock-Ah Im
Department of Internal Medicine, Seoul National University Hospital, Korea

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10:40-12:20 / October 12, 2007

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Dong Wha Lee Soonchunhyang University Hospital, Korea

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Department of Pathology, Yonsei University Medical College, Korea
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¹Department of Breast & Endocrine Surgery, Kumamoto City Hospital, Japan,
²Department of Clinical Pathology, Kumamoto City Hospital, Japan
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Department of Pathology, Inje University Sanggye Paik Hospital, Korea
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10:40-12:20 / October 12, 2007

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Ki-Keun Oh Yonsei University Yongdong Severance Hospital, Korea

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Department of Radiology, Seoul National University Hospital, Korea

Susan G. Komen for the Cure Luncheon

12:30-14:00 / October 12, 2007

Mugunghwa Grand Ballroom

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14:00-15:40 / October 12, 2007

Vista Hall I+II

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Johns Hopkins School of Public Health, Medicine and Nursing, USA
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College of Nursing, Seoul National University, Korea
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Kyum Koo Chon
Department of Health Promotion and Education, University of Utah, USA

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16:10-17:50 / October 12, 2007

Vista Hall I+II

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Sang Seol Jung The Catholic University of Korea, Kangnam St. Mary's Hospital, Korea

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Department of Surgery, Brigham and Women's Hospital Boston, USA
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¹Breast Center, Shandong Cancer Hospital, China, ²Breast Center, Beijing University Cancer Hospital, China,
³Department of Breast, Qingdao University 2nd Hospital, China, ⁴Breast Center, Zhongshan University 2nd Hospital, China,
⁵Department of Breast, Yantai Yuhuangding Hospital, China, ⁶Department of Breast, Shanghai Cancer Hospital, China,
⁷Department of Breast, Xuzhou Central Hospital, China, ⁸Department of Surgery, Beijing 307 Hospital, China,
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Department of Breast Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan

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16:10-17:50 / October 12, 2007

Grand Hall II+III

Moderators: Janice Bowie Johns Hopkins Bloomberg School of Public Health, USA
Pok Ja Oh Sahmyook University, Korea

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Graduate School of Public Health, Ajou University, Korea
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¹School of Nursing, The Hong Kong Polytechnic University, Hong Kong, China,
²School of Nursing, Department of Family Health Care Nursing, University of California San Francisco, USA

Symposium IX: Clinical Trials

16:10-17:50 / October 12, 2007

Vista Hall III

Moderators: Masakazu Toi Kyoto University, Japan
Yung-Jue Bang Seoul National University Hospital, Korea

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Kimberly L. Blackwell
Departments of Medicine and Radiation Oncology, Duke University Medical Center, USA

Dinner with Poster Discussion

18:00-20:00/ October 12, 2007

Grand Hall I

Panel V: Collaboration

08:30-10:10 / October 13, 2007

Vista Hall I+II

Moderator: Evaon Wong-Kim California State University, USA

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Johns Hopkins University, School of Medicine, USA
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Jong Koo Lee
Ministry of Health & Welfare, Korea Centers for Disease Control & Prevention, Korea

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10:40-12:20 / October 13, 2007

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Seung Jae Huh Samsung Medical Center, Korea

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¹Breast Oncology, National Kyushu Cancer Center, Japan,
²Psychooncology, National Kyushu Cancer Center, Japan
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10:40-12:20 / October 13, 2007

Vista Hall III

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Jung-Hyun Yang Samsung Medical Center, Korea

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Department of Surgery, University Malaya Medical Centre, Malaysia

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10:40-12:20 / October 13, 2007

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Byeong-Woo Park Yonsei University Severance Hospital, Korea

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Department of Surgery and Cancer Research Institute, Seoul National University College of Medicine, Korea
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Janet Price
Department of Cancer Biology, University of Texas M.D. Anderson Cancer Center, USA

Survival Session: Empower Yourself

10:40-12:20 / October 13, 2007

Mugunghwa Hall

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Myungsun Yi Seoul National University, Korea

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Breast Cancer Welfare Association, Malaysia
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Korea Breast Cancer Patients Society, Korea
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Japan Breast Cancer Network, Japan
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Taichung Kaihuai Association, Taiwan

Closing Ceremony

12:30-13:00 / October 13, 2007

Vista Hall I+II

Post-education Session I

14:00-17:00 / October 13, 2007

Vista Hall III

Post-education Session II

14:00-16:30 / October 13, 2007

Grand Hall II+III

Poster Discussion

October 11, 2007 (Thu)

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Shiraz University of Medical Science, Iran
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Department of Biology, Rasht-guilan University, Iran
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²Surgery, Kyung Hee University East-West Neo Medical Center, Korea
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Estonian Cancer Screening Foundation, Estonia
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¹Public Health, Faculty of Nursing and Midwifery, Iran, ²Medical-Surgical, Faculty of Nursing and Midwifery, Iran,
³Gynecology, Faculty of Medicine, Iran, ⁴Surgery, Faculty of Medicine, Iran
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College of Nursing, Nursing Policy Research Institute, Yonsei University, Korea
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¹College of Medicine, Cheju National University, Korea, ²Department of Nursing, Korea National Open University, Korea
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¹Surgery, Seoul National University Bundang Hospital, Korea,
²Gynecology, Seoul National University Bundang Hospital, Korea,
³Psychiatry, Seoul National University Bundang Hospital, Korea,
⁴Plastic Surgery, Seoul National University Bundang Hospital, Korea, ⁵Diagnostic Radiology, Seoul National University Bundang Hospital, Korea, ⁶Surgery, Seoul National University College of Medicine, Korea

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¹Surgery, Seoul National University College of Medicine, Korea,
²Surgery, College of Medicine, University of Ulsan and Asan Medical Center, Korea,
³Surgery, Soonchunhyang University, Korea,
⁴Therapeutic Radiology, Soonchunhyang University, Korea,
⁵Surgery, National Cancer Center, Korea,
⁶Medical Research Collaboration Center, Seoul National University College of Medicine, Korea
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¹Department of Surgery, University of Ulsan, Asan Medical Center, Korea,
²Department of Pathology, University of Ulsan, Asan Medical Center, Korea
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¹Department of Surgery, Seoul National University College of Medicine, Korea,
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²Department of Surgery, Seoul National University College of Medicine, Korea
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²Department of Pathology, Hallym University College of Medicine, Korea,
³Department of Pathology and Biomedical Research Center, Ulsan University Hospital, Korea
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¹Department of Radiation Oncology, Soonchunhyang University Hospital, Korea,
²Department of Surgery, Soonchunhyang University Hospital, Korea,
³Department of Hemato-oncology, Soonchunhyang University Hospital, Korea,
⁴Department of Surgery, Asan Medical Center, Korea,
⁵Department of Radiation Oncology, Cancer Institute of New Jersey, USA

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	¹ Department of Preventive Medicine, Seoul National University College of Medicine, Korea,	
	² Division of Cancer Epidemiology and Genetics, National Cancer Institute, USA,	
	³ Department of Epidemiology, Roswell Park Cancer Institute, USA,	
	⁴ DNA Link Inc., Korea,	
	⁵ Department of Surgery, Seoul National University College of Medicine, Korea,	
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	¹ Department of Preventive Medicine, Seoul National University College of Medicine, Korea,	
	² Division of Biostatistics, Graduate School of Public Health, Seoul National University, Korea,	
	³ Division of Cancer Epidemiology and Genetics, National Cancer Institute, USA,	
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	¹ Department of Preventive Medicine, Seoul National University College of Medicine, Korea,	
	² Department of Epidemiology, Roswell Park Cancer Institute, USA,	
	³ Division of Cancer Epidemiology and Genetics, National Cancer Institute, USA,	
	⁴ Department of Surgery, Seoul National University College of Medicine, Korea,	
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Global
Breast Cancer
Conference
2007

Panel

Clinical Characteristics and Survival Analysis of Korean Breast Cancer Patients

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Purpose: Breast cancer in Korea continues to rise year by year, but its clinical characteristics are different from Western countries. The purpose of this study is to evaluate the clinical characteristics and survival analysis of breast cancer patients in Korea using the nationwide data.

Methods: Since 1996, the Korean Breast Cancer Society has analyzed and reported the nationwide breast cancer data on a biannual basis. The Korean Breast Cancer Society has been collaborating with the Korean Central Cancer Registry to improve the completeness and validity of the breast cancer registry and the mortality data.

Results: The 5-year observed survival rate and the relative survival rate were 81.2% and 83.2%. This study showed a continuous increase in: the incidence of breast cancer, breast-conserving surgery, and breast reconstruction after operation, the percentage of early cancer and the number of patients with reproductive factors. In a difference from Western countries, the age distribution of Korean breast cancer peaked in the fourth decade of life. Younger patients (age <35 years) had tumors classed as higher T stage and higher LN positivity than older patients. The younger group also had significantly lower ER and PgR expression.

Conclusion: These results suggest that the rate of breast cancer in Korea is expected to continuously increase in the future. Several characteristics of Korean breast cancer patients seem to follow the patterns of Western countries, but differences are present. To understand the characteristics of Korea breast cancer, continuous nationwide data collection and analysis should be done.

Breast Cancer as a Public Health Problem

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Purpose: Worldwide, breast cancer is the most common cancer diagnosed among women and is the leading cause of cancer deaths. The purpose of this session is to provide an overview of the breast cancer statistics in the U.S. as well as worldwide. In addition, cancer health disparities among ethnic minority in the U.S. will be addressed.

Methods: Data on cancer mortality, incidence, and risk factors will be summarized by using the most recent data available from population-based cancer registries affiliated with the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) and CDC's National Program of Cancer Registries (NPCR). The California Health Interview Survey (CHIS) data will be also analyzed to provide the information on risk factors and screening behaviors

Results: Global differences in breast cancer incidence rates and fluctuations in rates within a country exist. The incidence of breast cancer in Asian countries was lower than in Western countries. Breast cancer incidence rates in the U.S. decreased each year during 1999-2003. On the other hand, the morbidity and mortality related to breast cancer has been strikingly increased in Asia.

Conclusion: Multidisciplinary strategies to reduce breast cancer mortality and promote breast cancer awareness will be addressed. Lessons learned from multidisciplinary approaches to cancer treatment and control will be valuable in implementing future breast cancer research in the fields of basic, clinical and population research in Asia.

Is it Breast Cancer a Different Disease in Asian Women?

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Breast cancer (BC) is one of the most common cancers in East Asian women. Although the incidence of BC is lower in East Asian women (Japanese, Korean, Taiwanese and Chinese) than Western women, it is increasing throughout East Asia. As a first step to determining whether BC therapies should be tailored differently for East Asian and Western women, the published literature on BC in East Asian women has been reviewed and compared to the present understanding of BC in women of European ancestry. The average age of BC onset is considerably lower in East Asian than Western women. The frequency of expression of hormone receptors in breast cancers in East Asian women appears to be lower, and the expression of ErbB2 higher, than in Western women. The differences in age of onset and frequency of hormone receptor expression suggest that BC may be more aggressive in East Asian women. The majority of BC molecular subtypes are observed in both Western and East Asian women. A similar spectrum of high and low penetrance genes have been associated with BC risk in East Asian and Western women, however, the frequency of specific deleterious alleles may vary. East Asian and Western women share common intrinsic and acquired risk factors for BC including hormone exposure, body mass index, alcohol consumption and diet. Although the intrinsic and acquired risk factors for BC are common to both East Asian and Western women, the relative exposure to these may vary according to a woman's ethnicity, culture and place of residence. These variations are expected to contribute to the differences in BC incidence between East Asian and Western women.

Translating Genetics to Cancer Prevention

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Purpose: Breast cancer is the most common malignancy in women living in industrialized countries. This disease includes two categories, hereditary breast cancer and sporadic breast cancer. It is estimated that germline mutations of some genes, such as BRCA1 and BRCA2, results in the development of approximately 5% of breast cancers. Various genetic and/or epigenetic changes in normal breast tissues are considered to result in the development of sporadic breast cancer.

Results: Recently, a number of studies have been performed to investigate novel molecular classifications of breast cancer using gene expression profiling. One of these classifications, the 'intrinsic subtype' model, is associated with the origins of breast tumors, endocrine-responsiveness and HER2 status. An immunohistochemical (IHC) profile for ER, progesterone receptor, HER2, HER1 and cytokeratin 5/6 using formalin-fixed, paraffin-embedded samples was developed and verified against a gene expression profile in the 'intrinsic subtype' model. It has been suggested that a higher prevalence of the basal-like subtype exhibiting aggressive phenotypes contributes to a poorer prognosis for African American breast cancer patients. We have also found that a lower prevalence of the basal-like subtype contributes to a favorable prognosis for Japanese breast cancer patients. Interestingly, epidemiological and experimental studies have suggested that a high intake of green tea reduces the overall incidence of breast cancer and also more efficiently reduces the incidence of basal-like breast cancer.

Conclusion: The genetic and epigenetic backgrounds of breast cancer carcinogenesis and chemopreventive strategies against both ER-positive and ER-negative breast cancer will be reviewed and discussed in this lecture.

Preventive Choices for High Risk Women Based on Gene-Environment Interaction of Breast Cancer

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Breast cancer is the most common cancer among women worldwide. According to the World Health Organization, more than 1.2 million people will be diagnosed with breast cancer this year worldwide. The American Cancer Society estimates that in 2004, approximately 215,990 women in the United States were diagnosed with invasive breast cancer. The major risk factor for breast cancer can be traced to reproductive events that influence the lifetime levels of hormones. However, a large percentage of breast cancer cases cannot be explained by these risk factors. The identification of susceptibility factors that predispose individuals to breast cancer (for instance, if they are exposed to particular environmental agents) could possibly give further insight into the etiology of this malignancy and provide targets for the future preventive intervention. The most interesting candidate genes are low penetrance genes with common polymorphisms, which include carcinogen metabolism, steroid hormone metabolism, DNA repair, signal transduction and inflammatory process, and cell cycle controls.

Three preventive strategies will be discussed based on the findings of the gene-environment interaction of breast cancer from the studies conducted in Korea where the incidence of breast cancer is still relatively lower and the demographical characteristics and personal habits are different from the rest of the world. These include behavior modification (e.g., caloric restriction, dietary intervention, etc.) for high risk subjects (primary prevention), early detection and extensive monitoring of genetically susceptible subjects and noninvasive treatment of early stage cancer cases (secondary prevention), and finally prophylactic and therapeutic intervention to slow the progression of diseases (tertiary prevention).

We have conducted a case-control study in Korea to evaluate the potential modifying roles of the genetic polymorphisms of selected low penetrance genes that are involved in carcinogen metabolisms (i.e., GSTM1/T1/P1, NAT1/2, CYP1A1, CYP2E1, EPHX, NQO1, ALDH2), estrogen synthesis and metabolism (i.e., ER- α , CYP1A1, CYP1B1, CYP17, CYP19, COMT, SULT1E1/1A1), DNA repair (i.e., hOGG1, XRCC1/2/3/4/6, ERCC1/2/4, ATM, AGT, LIG1/4, RAD51/52, hMLH1), and signal transduction and inflammatory process (i.e., TGF- β 1, TNF- β , IGF1, IL1B, IL1RN, HER2), and cell cycle control and others (i.e., CCND1, CDK7, BCL-6, BAR2, MTHFR) in breast cancer. We also took into account the potential interaction between these SNPs and the

known risk factors of breast cancer. Histologically confirmed incident breast cancer cases (n=1,467) and controls (n=1,615) with no present or previous history of cancer were recruited from several teaching hospitals in Seoul during 1995-2003. Genetic polymorphisms were determined by PCR, PCR-RFLP, real-time PCR, DASH, PCR-CTPP, MALDI-TOF mass spectrometry, and 5'-nuclease assay (TaqMan).

Profiles of risk factors are similar with the findings from the countries with higher incidence of breast cancer. Higher education, positive family history of breast cancer in the first and second degree relatives, alcohol drinking, cigarette smoking, lifetime cumulative estrogen exposure, use of oral contraceptives, and higher paternal age when a subject was born were significantly associated with breast cancer. Several dietary factors (e.g., soybean, vitamin A, folate intake, etc.) are associated with decreased risk of breast cancer.

We have found the remarkable ethnic difference in the distribution of genotype frequencies; the ATM 1066-GT/G, Ser707Pro, AGT Ile143Val, Gly160Arg, XRCC2 31479G/A, XRCC6 1796G/T, LIG4 1997T/C, and CDK7 99T/C were not polymorphic in Korean population whereas the frequencies of minor alleles in Caucasian were relatively high.

The genetic polymorphisms of some selected low penetrance genes (e.g., GSTM1/T1 null, GSTP1 105Val, CYP2E1 c1/c1, NQO1 187Ser, XRCC1 399Gln, RAD52 2259T, ERCC1 8092A, hMLH1 -93G, ER XbaI xx, COMT-L, CYP19 264Cys, SULT1E1 949A, TGF- β 1 29T, TNF- β 252G, CCND1 870A, and MTHFR 667C) are associated with the risk of breast cancer development. The significant gene-environment interaction is also observed between selected SNPs and known risk factors (e.g., alcohol drinking, lifetime exposure to estrogen, etc). Ever-drinking women with the CYP2E1 c2 allele containing genotypes had a 1.9-fold risk for developing breast cancer compared to never-drinkers with the CYP2E1 c1/c1 genotype (p for interaction=0.04). There was a significant multiplicative interaction between ER α 1782A/G genotypes and lifetime exposure to estrogen in breast cancer development (p for interaction=0.02).

The recent advance in our studies includes the haplotype and/or diplotype analysis, the identification of SNPs associated with clinico-pathological characteristics and prognosis/survival, and the determination of the genotype-phenotype relationship for DNA repair genes and DNA repair capacity. As the number of ATM ATGTG haplotype decreased, which consisted of 5144A/T, IVS21+1049T/C, IVS33-55T/C, IVS34+60G/A, and 3393T/G polymorphisms, the risk of breast cancer increased (p-for trend <0.01). Breast cancer cases with SULT1E1 IVS4-1653 TC or CC genotypes showed approximately 3-fold increased risk of recurrence (HR=3.2, 95% CI=1.39-7.48) compared to those with TT genotype among cases undertaken surgery.

Novel and Intraductal Approaches to Chemoprevention of Breast Cancer

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Purpose: Unlike historical trial requiring thousands of patients and many years of follow-up, we are pursuing newer clinical models utilizing candidate surrogate biomarkers of drug activity that permit screening studies with smaller sample sizes and brief duration of drug exposure. Promising agents can then be taken to large-scale, definitive clinical trials. The current options for breast cancer prevention are limited to a mastectomy or 5 years of tamoxifen. Because breast lesions originate in the epithelium lining the ducts, we hypothesized that strategies to eliminate ductal pre-malignant lesions may prevent breast cancer. Based on our strong preclinical data (Cancer Res, 66, 638, 2006), we proposed that it is feasible and safe to administer intraductal pegylated liposomal doxorubicin (PLD) into breast ducts of women with breast cancer.

Methods: To test this concept, we are performing a phase I clinical trial to evaluate, 1) the feasibility, safety, and maximum tolerated dose of PLD administered into one breast duct of women with breast cancer awaiting a mastectomy, and 2) the local and systemic exposure of PLD by serial determination of doxorubicin and doxorubicinol concentrations in plasma, in nipple aspirate fluid, and in breast tissue at the time of mastectomy.

Results: Six women have been entered into the trial. The procedure is feasible in the out patient setting, well tolerated, and local and systemic toxicity for 2 mg PLD are low.

Conclusion: The long-term goal is to eradicate pre-malignant or non-invasive breast lesions and ultimately prevent breast cancer in women with a high risk of developing breast cancer.

Promotion of Mammography: What Can Be Learned from the U.S. Experience?

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Purpose: The purpose of this session is to provide an overview of the U.S. experience in promoting screening mammography. Trends in mammography uptake and the many factors that influence use of screening tests, such as a woman's socioeconomic status, health care provider referral for mammography and the organization of health care delivery will be examined. Lessons learned from conducting interventions to promote mammography will be described as they relate to implications for different systems of health care delivery.

Methods: Evidence from the accumulated literature on strategies to promote mammography adherence will be summarized.

Results: High rates of mammography uptake have been achieved in the U.S. despite the fact that there is no centrally organized method of delivering screening services. However, these high rates of screening are not evenly distributed across the eligible population. Interventions that have worked to increase screening include strategies such as physician and patient reminders, access enhancements, tailoring interventions to individual barriers and reorganizing the delivery of health services. Strategies to improve adherence to screening may be more effective if they are commensurate with how widely the test has been accepted and adopted by the population.

Conclusion: Multi-component interventions that address a combination of individual, social and structural factors can improve rates of screening. Although high rates of screening mammography have been achieved in the U.S., population disparities in use continue to exist. Targeted efforts can reduce disparities, but these strategies are not routinely implemented in routine practice.

Surgical Treatment: Controversies and Challenges in Surgical Treatment for Early Breast Cancer

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Because of recent changes in concepts on cancer metastasis, the development of radiologic equipment, and the introduction of randomized clinical trials, the operative methods of breast cancer patients is changing.

Breast conserving surgery and sentinel lymph node biopsy is becoming more and more common. We wish to describe the many controversies that exist over these new methods. Breast conserving surgery is considered now to be the appropriate operative method for early breast cancer patients. But the choice between lumpectomy and quadrantectomy is still controversial. Also, the standard on resection margin, the factor most associated with post operative local recurrence, is different from each clinical research centers and from each doctor. A common standard is needed.

Sentinel lymph node biopsy is a safe and accurate method of finding out whether an axillary lymph node metastasis exists in early breast cancer patients. But the report on its identification rate and false negative rate is varied, and need to be standardized. The choice of tracers (blue dye/radioisotope) and injection sites (peritumoral, dermal, sub-aureolar) is also a matter of argument.

Compared with conventional mastectomy, the skin sparing mastectomy has many advantages, such as excellent aesthetic effects, the increase of the quality of life, and the reduction of psychological trauma. But there is great controversy over the matter of dermal recurrence. Also, the interest in the preservation of nipples has led to an increase of research in the risk factors of nipple involvement.

Lively debate on methods of breast cancer surgery will lead to customized surgery fitting each patient individually, and with it, the development of breast cancer surgery and the increase of the patient's quality of life will advance tremendously.

Adjuvant Clinical Trials Overview; Optimizing Chemo/Endocrine Therapy to Individualized Patients

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During the past two decades, accumulation of incremental benefits from systemic adjuvant chemo/endocrine therapy has improved the outcome of patients diagnosed with early stage breast cancer dramatically. However, over-treatment has become an issue. For example if chemotherapy is given to all ER+ N- patients in addition to tamoxifen, about 85% would be over-treated. Since treatment decision is based on assessment of base line risk of failure as well as expected degree of benefit from therapy, context specific prognostic markers would be useful. Tools such as Adjuvant On Line based on clinicopathological variables are useful but assumes equal benefit from chemotherapy in all risk categories and also suffers from dependency on tumor grade which is not highly reproducible. Risk estimate also is not a linear function. A mutagen based assessment of base risk (OncotypeDx Recurrence Score) provides continuous estimate of risk after tamoxifen treatment in N-ER+ patients (Paik et al, NEJM, 351:2817). Furthermore, linear relationship between OncotypeDx Recurrence Score and degree of benefit from chemotherapy (Paik et al, JCO, 24:3726) provides a rationale of using Recurrence Score as a clinical decision making tool. However due to continuous nature of the Recurrence Score, degree of benefit from chemotherapy in those with intermediate risk category is not clear and is a subject of a large clinical trial in US (TAILORx trial).

Residual risk assessment after chemotherapy is another important context when considering design of trials for targeted therapies. Problem is that as suggested by data from NSABP B-20, there is a link between poor prognosis and response to chemotherapy and simple use of prognostic factors does not provide effective tools to identify those with high residual risk after chemotherapy. Data from NSABP B-27 suggests that combination of gene expression profile with response to neoadjuvant therapy may provide tools to identify those at high risk of failure even after chemotherapy among those with inherently poor prognosis.

Use of context specific prognostic factors in designing clinical trials is expected to decrease the required sample size for clinical trials and provide ideal setting to test newer regimens for the treatment of breast cancer.

Breaking News about On-going Clinical Trials

Jo Anne Zujewski¹

¹*National Cancer Institute, USA*

Purpose: In the United States, the 5 year relative Disease Free Survival (DFS) in breast cancer has improved from 75% in 1974-76 to 88.6% in 1996-2003. Improvement is due, in part, to increased use of adjuvant systemic therapies. A major new development is the use of genetic profiling to identify multiple subtypes of breast cancer. Thus, the National Cancer Institute clinical trials portfolio has incorporated trials of ‘tailored’ therapy directed towards individual subtypes.

Methods: Treatment approaches include integrating new agents into standard regimens, comparing two or more novel approaches, multimodality treatments, incorporating correlative sciences and banking tissues, and studying less common presentations of common diseases. Harmonized processes for tissue collection and endpoint nomenclature have been developed through international collaborations.

Results: The TAILORx trial incorporates the use of a molecular profiling tool (OncotypeDX) to randomize patients to chemotherapy and hormonal therapy versus hormonal therapy alone for lymph node negative hormone receptor positive breast cancer. This trial complements the MINDACT trial conducted by the Breast International Group. Studies using novel agents (lapatinib, bevacizumab) are being conducting in both the pre-operative and adjuvant setting in specific molecular subtypes, thus allowing for more detailed correlative science studies in conjunction with preliminary efficacy and safety studies. Trials are planned to examine the role of novel therapeutics in patients with residual disease (and thus at increased risk of recurrence) post neo-adjuvant chemotherapy.

Conclusion: Future efforts will include international clinical trial and correlative science efforts as well as focusing on uncommon presentations of breast cancer.

How and Why Patient-oncologist Communication Matters in Breast Cancer

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Purpose: The purpose of this presentation is to provide a brief review of the state of the art in regards to the bioethical and evidence base relating patient oncologist communication to patients' quality of life.

Methods: The terrible stress of a breast cancer diagnosis is made even worse by the confusing array of treatment options. Further intensifying the challenge of decision-making is that most women with breast cancer are incompletely informed about their prognosis and commonly overestimate risks as well as treatment benefits. Since physicians' communication of both emotional support and clinical information to patients is limited, patient fears and misperceptions often go unrecognized and unaddressed by physicians. Furthermore, there is wide variation in patient preferences, experience, and capacity to process complex information and engage in the decision-making process. The growing mandate to assure skillful, patient-centered communication in oncology can be linked to a variety of societal concerns that cross cultural boundaries. These include: (a) a quality of care perspective which increasingly focuses on an evidence base linking effective communication to clinically significant patient outcomes and physician well being; (b) recognition of the role of communication in enhancing the therapeutic power of the patient-physician relationship; and, (c) deepening appreciation for the role of collaborative decision making to go beyond protection of patient autonomy to building therapeutic partnerships.

Results: Communication skills training for physicians and activation interventions for patients and their families show promise in optimizing the therapeutic effect of the patient-physician relationship and contributing to greater quality of life for breast cancer patients.

Needs of Korean Women with Breast Cancer and their Quality of Life

Myungsun Yi¹

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Purpose: The purpose of this session is to present the informational needs of Korean women with breast cancer (KWBC) and how to improve their quality of life.

Results: As many studies in Western societies have indicated, KWBC also have distinct needs for information throughout their breast cancer journey. Newly diagnosed women need information concerning potential prognosis, the likelihood of cure, treatment options, the stage of disease as well as the etiology and how they should have prevented the cancer. In the treatment stage with surgery, potential problems after the surgery, self-care, changes in the wound region, and treatment options other than surgery were the most needed information. In the stage of chemotherapy, the women needed information about survival rate, prognosis, and complications/side effects of chemotherapy. During the radiation therapy, they wanted to know why radiation was needed, about the kinds of complications/side effects and when they would occur. In life after the treatment, they needed wide range of information concerning the possibility of recurrence, lymph-edema, how to relieve anxiety/fear of recurrence, fatigue, pain, and about nutrition, exercise, and alternative medicine. In terms of quality of life among KWBC, the highest scoring domain was the spiritual domain, while the psychological domain was the lowest, due to the anxiety/fear of recurrence and metastasis.

Conclusion: It is important for health professionals to provide education in accordance with patients' self-identified needs based on the specific period of the illness journey, and to provide counseling to promote psychological well-being for KWBC.

Emotional Well-being for People with Breast Cancer

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In this presentation, I will first provide a control theory approach to the quality of life and emotional well-being. According to the model, the quality of life consists of five components (environment, motivator, detector, controller, and effector) at four levels (physical, psychological, social, and spiritual). Well-being is defined as the congruence between the actual state measured by the detector and the desired state provided by the motivator at each level (e.g., physical well-being, spiritual well-being). From a hierarchical control standpoint, emotional well-being is the proximate factor to (ill) health, whereas the above four well-beings, except physical well-being, are distant factors to (ill) health. From a cognitive control standpoint, three magic bullets — gratitude (past perfect), happiness (present), and hope (future) — and three black magics — depression (past perfect), anger (present), and anxiety (future) — appear to be critical for breast cancer patients. The second part of the presentation delineates how to assess and to promote emotional well-being, focusing on magic bullets, for breast cancer patients. According to the model, we need to assess at least three components: need (motivator), perception (detector), and coping capacity (effector). With respect to the promotion of emotional well-being, there are three groups of coping styles at motivator (e.g., resignation), detector (e.g., diversion), and effector (e.g., active coping). In addition, there are specific strategies to promote gratitude (e.g., downward comparison), happiness (e.g., small is beautiful), and hope (e.g., possibilities rather than limits). Finally, more detailed discussions (e.g., false hope) will be presented at the Conference.

Partnerships for Cancer Control and Prevention: The Sidney Kimmel Comprehensive Cancer Center and the State of Maryland

Norma Kanarek¹

¹*Cigarette Restitution Fund Program at JHMI, USA*

In the Tobacco suit launched by states' attorneys general, Maryland was awarded \$60 million/year for 30 years. Much of this award has been dedicated to health, including medical care services. In addition, the spending plan included local and state cancer control programs, state and local tobacco cessation and prevention activities, and cancer research at its two academic medical centers.

Since 2000, the Johns Hopkins Medical Institutions (Schools of Medicine, Nursing, and Public Health) has received research dollars from the state and funded eighty research projects or faculty recruitment and retention awards. These activities were selected based on scientific merit and state and local priorities. The projects span basic, clinical and population-based studies; nursing, medicine, and public health; biostatistics, epidemiology, health policy, environmental health sciences, and genomics. High priority goes to research that addresses a Maryland problem, health disparities, and priority cancers.

The CRF Research Grant at SKCCC has augmented cancer prevention and control research and fostered a collaborative environment in cancer research between the two academic centers. Overall, Maryland's cancer statistics have experienced positive changes over the last decade.

Clinicians' Point of View

Kwang-Man Lee¹

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The breast is the single most frequent site of cancer among women in the western countries, and efforts to control breast cancer is one of national priorities in those countries. Unfortunately, the incidence of breast cancer is increasing steadily in East Asian countries, and actually breast cancer has been the most frequent female cancer in Korea since 2002. Nowadays, cancer is no longer regarded as an acute illness but as a chronic and complex disease requiring a myriad of treatment, a lot of support services and life-long follow-up. Cancer treatment has increasingly moved out of the hospital and into the community. The goal of cancer treatment can be achieved primarily by a multi-disciplinary health care team comprised of clinicians, psychologists, nurses, physical therapists, dieticians, and spiritual carers. And cooperation between clinician and researchers is also important. Furthermore, to achieve long-term survival and maximum quality of life, support from the community is crucial, and it should begin at the time of diagnosis and continue throughout the treatment course and life. In recent years, the cooperation between the government and medicine is critical to the cancer research and treatment. Actually the most important sponsor of medical research has been the government. Moreover, policies regarding health insurance have a tremendous influence on cancer treatment. And cancer survivors or self-help groups may be a voice for political action on research funding and health insurance coverage. Close cooperation between clinicians, patients, researchers, and policy makers is crucial for the future of cancer research and treatment.

Advocates' Point of View

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In the United States, breast cancer advocates have numerous opportunities to collaborate with researchers, health care providers, cancer patients and policy makers to assure comprehensive breast cancer control. Many advocates have had first hand experience with breast cancer. These advocates are committed to increasing awareness about breast cancer, enhancing understanding of the disease and its treatments and improving quality of life of people with breast cancer. Through collaboration with policy makers, advocates play a key role in obtaining federal and local funds for breast cancer research and treatment. Advocates also participate in the research grant proposal review process as consumers, representing the perspectives of patients, survivors and family members. The critical issues for women with breast cancer include informational needs, patient-physician communication, psychosocial issues, choice in primary surgical treatment, in reconstructive surgery, and in adjuvant therapy, and employment and insurance concerns. Both health care workers and advocates can play an important role in addressing these issues. Health care providers and hospital systems often contact advocacy programs such as 'Reach To Recovery' to assist newly diagnosed breast cancer patients. Having had first hand experience with breast cancer, advocates are in an excellent position to offer support to breast cancer patients and their caregivers. We can accomplish far more when we share our knowledge and experience and collaborate to promote breast cancer research, to enhance understanding of breast cancer and its treatments, and to improve quality of life in breast cancer patients all of which bring us closer to a cure.

Patients' Point of View – Patient Focused Care – Who is the Most Important Health Care Provider to the Patient?

Lillie Shockney¹

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Purpose: Provide the audience a personal understanding of the role each health care professional has in the diagnosis, care and treatment of a breast cancer patient, through the eyes of a patient.

Methods: Verbally present a patient's experience from the beginning of the journey with diagnosis through to the end of treatment and describe (verbal presentation) and show (short video) that depicts a patient's experience and her dependence on each and every person involved in her care. (Example: the pathologist, who the patient never meets, is responsible for accurately diagnosing her, determining the stage of her disease and the prognostic factors because without this information being accurate she may be under or overtreated.)

Results: We under-estimate the roles we each play in the life of a breast cancer patient. We each need to take pride in knowing our importance to her at any given time.

Conclusion: We see thousands of breast cancer patients; the patient only sees one of us. She will remember us if we helped her and did our job well; she will remember us if we failed her.

Sector-wide Approaches in National Cancer Control Program in Korea

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Purpose: To review of Korean government's cancer control policy and know how to make close collaboration with several sectors to reduce the burden of cancer in Korea.

Methods: According to 1st and 2nd National Comprehensive Cancer Control Plan, the accomplishment and future directions of Korean government's policies on cancer were reviewed by experts with input, process, output indicators.

Results: Korean government initiated the 1st and 2nd National Comprehensive Cancer Control Plan in 1996, 2006. According to the 1st Plan, Korea set up an infrastructure system against cancer, for examples construction of the National Cancer Center, designation of 9 Regional Cancer Centers, enforcement of Cancer Control Act and embarkation of national cancer screening programs including stomach, cervix and breast cancer. So, Korean government made close collaborations with NGO sectors to improve the public awareness and understanding of cancer prevention, early detection, screening to improve participation rate of 'screening' and '10 Codes of Conducts for Cancer Prevention', for examples 'Education program in the local province', 'Pink Ribbon Campaign'. In the near future, Korean government will make a build-up of national framework for cancer surveillance from risk factors in general population to quality of life in cancer patients with sector-wide collaboration networks.

Conclusion: To accomplish the 2nd Plan, close collaboration with professional, private and NGO sectors became more important driving force for dissemination into action of evidence-based national cancer control policies especially in the field of prevention, early detection and screening based on the infrastructure system.



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Strategies for the Use of Adjuvant Aromatase Inhibitors

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Third-generation aromatase inhibitors (AIs) are highly potent and selective in suppressing whole-body production of estrogens in postmenopausal women. However, letrozole reduces levels of estrogens to a greater degree than the other AIs, anastrozole and exemestane. Most importantly, this greater suppression of estrogens includes estradiol, the most bioactive estrogen with regard to stimulating proliferation, down-regulating apoptosis, and promoting expression of metastasis-related biomarkers in breast cancer cell lines. In direct and indirect clinical comparisons of AI trials in postmenopausal women with hormone-responsive breast cancer, letrozole has consistently achieved greater efficacy than anastrozole or exemestane, reflecting this increased potency. The greater relative efficacy of letrozole has been seen in first- and second-line treatment for metastatic disease, neoadjuvant therapy, initial adjuvant therapy for 5 years, and extended adjuvant therapy after 5 years of adjuvant tamoxifen.

In separate large randomized phase III initial adjuvant trials, both letrozole (in Breast International Group trial BIG 1-98) and anastrozole (in the Arimidex[®], Tamoxifen, Alone or in Combination [ATAC] trial) were significantly more efficacious than tamoxifen in reducing the risk of recurrence. In BIG 1-98 at a median follow-up of 26 months, letrozole significantly increased disease-free survival (DFS) (hazard ratio [HR] 0.81, $p=0.003$) and time-to-recurrence (HR 0.72, $p=0.001$) compared with tamoxifen. In the ATAC trial (median follow-up: 68 months), anastrozole achieved a comparable improvement in DFS (HR 0.83, $p=0.005$) and time-to-recurrence (HR 0.74, $p=0.0002$) than tamoxifen. However, with letrozole there was also a greater improvement in time-to-distant recurrence than with anastrozole (HR 0.73, $p=0.001$ vs. HR 0.84, $p=0.06$, respectively). Although overall survival was not significantly improved in either trial, a greater relative improvement was seen with letrozole (HR 0.86, $p=0.16$) than with anastrozole (HR 0.97, $p=0.7$). Differences in efficacy in select patient populations were also seen in these two trials, in subgroup analyses. In BIG 1-98, letrozole was more effective, relative to tamoxifen, in patients who were node-positive and in those who received prior chemotherapy; in contrast, anastrozole was most effective compared with tamoxifen in patients with node-negative tumors, and in chemotherapy-naïve patients. These trial differences suggest that letrozole may provide greater benefit for patients with a high risk of recurrence, especially early distant recurrence.

The FACE trial (Femara vs. Anastrozole Clinical Evaluation) is directly comparing initial adjuvant therapy with letrozole vs anastrozole to determine whether letrozole shows greater benefits in postmenopausal patients with node-positive, hormone-responsive early breast cancer. This trial is a randomized multi-centered study enrolling approximately 4,000 postmenopausal women in more than 250 global sites. Patients will receive either 2.5 mg of letrozole or 1 mg anastrozole per day for the duration of 5 years or until recurrence. The primary endpoint is DFS. Secondary endpoints for efficacy include: distant DFS, time to distant metastasis, time to contralateral breast cancer, and overall survival. Safety analysis will include alterations of serum lipids, and rates of bone fracture and cardiovascular events. The FACE trial is the first head-to-head comparison of letrozole and anastrozole as adjuvant therapy and should establish definitively whether the greater potency of letrozole in suppressing estrogen production translates into greater efficacy in this vital treatment setting.

Adjuvant Hormonal Therapy for Premenopausal Women: The Need of Multinational Trial in Asian Countries

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Almost 60% of newly diagnosed invasive breast cancers occur in women under 50 years of age in Asia, and more than half of them are hormone responsive tumors. While there has been rapid and outstanding progress in adjuvant endocrine treatment for postmenopausal women through the use of aromatase inhibitor, clinical trials regarding endocrine therapy for premenopausal women are not yet sufficient, and most of these trials have potential limitations.

We have several options available for endocrine therapy for premenopausal women, including (1) cytotoxic chemotherapy; (2) selective estrogen receptor modulator like tamoxifen; (3) estrogen deprivation strategies such as permanent ovarian ablation or reversible suppression using LHRH agonists. However, there is uncertainty about how best implement adjuvant endocrine therapy to individual young patients using tamoxifen and estrogen deprivation as well as how to integrate these approaches with chemotherapy.

Tamoxifen remains the standard adjuvant endocrine therapy. Ovarian suppression also has shown great efficacy. Because ovarian suppression as a systemic therapy is associated with considerable side effects, it should be used under the firm evidence for survival benefits outweighing corresponding adverse effects.

In this presentation, based on results of clinical trials and meta-analyses available, following specific questions regarding adjuvant endocrine therapy for premenopausal women will be addressed, and a clinical trial for addressing some unanswered questions will be proposed.

1. Is tamoxifen also effective to very young patients (<35 years)?
2. Is ovarian suppression superior to tamoxifen in very young patients (<35 years)?
3. Do aromatase inhibitors play a role to young women who become menopausal after cytotoxic chemotherapy?
4. Can ovarian suppression be an alternative to chemotherapy in premenopausal HR+ patients?
5. Does the addition of ovarian suppression to standard treatment (chemotherapy + tamoxifen) provide extra benefits in premenopausal HR+ patients?
6. Does the addition of ovarian suppression provide extra-benefits to those who remain premenopausal or regain the menstruation after cytotoxic chemotherapy?

Neoadjuvant Hormonal Therapy for Breast Cancer

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Purpose: Neoadjuvant therapy is currently used as systemic treatment for early breast cancer. The novel treatment armamentarium provides more opportunities for patients undergoing breast conserving therapy and thorough study of biologic markers influencing the tumor response. Estrogen receptor (ER), progesterone receptor (PgR), or both positive breast tumors have been proven to be one of the important factors strongly associated with the development of cancer. Blockage of estrogenic signaling is the foundation of management for ER and/or PgR positive breast cancer.

Methods: Neoadjuvant hormonal therapy is indeed an alternative for postmenopausal patients unfit for neoadjuvant chemotherapy. However, recent research on neoadjuvant hormonal therapy showed low pathologic complete response (pCR) rate which is a well-adopted prognostic surrogate marker.

Results: Only less than 10% of patients receiving 3-month neoadjuvant tamoxifen or aromatase inhibitors (AIs) obtained pCR. Moreover, resistance to hormonal therapy is commonly observed. Combination with other cytotoxic chemotherapy or signal transduction inhibitors would be considered for future novel systemic therapy. Nevertheless, some studies demonstrated that pCR rates of patients with ER positive breast tumors were significantly lower than that of patients with ER negative breast tumors.

Conclusion: Signal transduction inhibitors could therefore be considerable options. Its ability to inhibit other ER signaling pathways could importantly augment the anti-proliferative effect of hormonally therapy. More studies on the combination of hormonal therapy with signal transduction inhibitor are noteworthy to search for better regimens.

Developing Molecular Markers for Targeted Therapy

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Even though several molecular targeted agents (MTA) have been introduced in the clinic, the efficacy was heterogeneous and the target specific response prediction is not possible. In addition to the clinical variables, the genetic differences of the tumor tissues and the host play a significant role in diverse efficacy and toxicity to MTAs. As the biology and genomics are improved, the treatment based on the predictive pharmacogenomics becomes one of the significant approaches for the personalized therapy, resulting in maximizing the efficacy and minimizing the toxicity of each patient. Therefore the functional pharmacogenomics using the current high-throughput technology become significant in MTA drug development; 1) to understand the mechanism of action of the drug, 2) to identify the reliable predictive biomarkers based on the genome wide approach, 3) to understand the mechanism of drug resistance, and 4) to develop the safe and effective dosing and schedule based on proper molecular targeting. We applied functional pharmacogenomics using cDNA microarray technology in several model systems to understand the mechanism of action, and to identify the proper patient for the better efficacy with minimal toxicity. With the different functional pharmacogenomic approaches, the proper integration of various markers combined with the clinicopathological parameters give the more accurate and reliable prediction power not only for the biological MTAs but also for the cytotoxic agents. In summary, current approaches enabled us one step forward to individualized treatment in targeting specific tumors and selection of proper patient who can get the best benefit/risk ratio from the treatment.

Prediction of Future Occurrence and Probability of Developing Breast Cancer over Lifespan in Korean Women

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The Gail model for predicting absolute risk of breast cancer has been used for counseling and to design intervention studies in western countries. Although it has been validated in U.S. women, its performance in other populations is still unclear. Among Korean women, breast cancer incidence is lower than among U.S. women, while mortality is higher. Moreover, there is a big difference in age-specific incidence rates between Korea and U.S.A. Therefore, we need a new model fitted in Korean women. We used data from a multicenter case-control study to select Korean major risk factors. A model of relative risks for various combinations of Korean major risk factors was developed. Since the rates are different between women under age 50 and those of age 50 or more, we selected two different models according to cut-off age of 50. We calculated individualized breast cancer probabilities from information on relative risks and the baseline hazard rate using Gail's equations. Due to lower baseline hazard rate and relative risks, the future breast cancer probabilities were much lower in Korean than in U.S. women. When we added some genetic factors in that model, the test performance of the model was increased. Our model may be useful for Korean women to predict the future absolute risk without overestimation when we use Gail model. This model will be further validated in Korean Cohort studies.

The Current Status of Breast Cancer Diagnosis and Treatments in China

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Purpose: To illuminate the current status of breast cancer diagnosis and treatments in China.

Methods: By reviewing the data of breast cancer diagnosis and treatments in China.

Results: The proportion of early-stage breast cancer is increasing from 74% in 1990 to 90% after 2000; DCIS is from 1.8% in 1990 to 14% in 2005. The peak of on-set ages is 45-50 year-old. Procedures commonly used in diagnosis are physical examination, mammography, ultrasonography and so on. Fiberoptic ductoscopy system (FDS) has been introduced for nipple discharge since 1990s. It indicated that FDS have potential use in minimally invasive treatment of small central papillomas. The proportion of breast-conserving surgery (BCS) is 15%-30% in leading hospitals. Reconstruction following mastectomy as an alternative to BCS is available now. Modified radical mastectomy remains the most used (70~80%) surgical modality. The prevalence of sentinel lymph nodes biopsy is less than 5%. Anthracycline-based chemotherapy regimen gradually takes the place of CMF from 1990, and now becomes the most-used regimen. The taxane-containing regimen is used for nodes positive disease. Several multiple-central clinical trails have been conducted to confirm the efficacy and safety of new regimens in an adjuvant setting. The combined treatments of LHRH-a with aromatase inhibitors or TAM seem to be more significant for Chinese patients, most of whom (~56%) are premenopausal. The 5-year DFS is 76.5%, 5-years OS is 87.6%.

Conclusion: The diagnosis and treatments of breast cancer in China is developing rapidly in last decade, catching up the international trends.

Assessing the Economic Burden of Breast Cancer in a National Cancer Center Managed Care Patients

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To estimate the economic burden of breast cancer, we examined direct and indirect cost in a prospective breast cancer cohort at the National Cancer Center (NCC), Korea. We estimated the total cost of breast cancer in 161 newly diagnosed patients and identified the major factors affecting this value. Direct costs included all healthcare costs, transportation, cost for alternative medicine and assistant. They were assessed every 3 months over a 24-month period through patient interviews, medical records and claims data. Indirect cost was replaced by the cost associated with lost or impaired ability to work or engage in leisure activities and lost economic productivity due to death attributable to the disease. The average annual direct cost per patient during the first and the second years after diagnosis were \$18,323 and \$2,635 (USD), respectively. In the multiple regression models, direct costs were significantly higher in highly educated patients diagnosed with advanced breast cancer (stage III/IV) who underwent surgery with radiotherapy and/or chemotherapy + hormonal therapy, and subsequently suffered a recurrence and/or death. These results demonstrated that that the breast cancer treatment was associated with substantial economic burden especially in the advanced stages. The prevention or early detection could be the best strategy not only for cost reduction but also for best outcome.

Genetic Counseling and Its Implications for Breast Cancer Prevention

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Purpose: Mutations in BRCA1/2 account for up to 90% of families with hereditary breast and ovarian cancer. Women with mutations have an estimated 40-87% chance of developing breast cancer and a 16-60% chance of developing ovarian cancer. Genetic testing can provide a more accurate estimation of an individual's risk, perhaps allowing for the adoption of appropriate risk-reducing strategies. Studies have shown that prophylactic mastectomy and oophorectomy reduce the risk of breast and/or ovarian cancer in BRCA1/2 carriers. Other recommendations for primary and secondary prevention include screening and chemoprevention, although evidence is insufficient to support their effectiveness in BRCA1/2 carriers. Genetic counseling, including risk assessment, education, and counseling to promote informed choice, adaptation to risk, and consideration of cancer prevention strategies, is an essential component of the testing process. Studies of cancer genetic counseling have shown post-counseling increases in knowledge and accuracy of risk perception, and decreases in cancer worries and decisional conflict related to chemoprevention decisions.

Results: Variations in genetic counselors' attention to the psychosocial implications of testing, focus on emotions, language use, communication interactivity, type of risk presentation, and expression of empathy have been associated with outcomes such as patient knowledge, accuracy of risk perception, post-counseling satisfaction, and affective state. These intermediate outcomes may affect subsequent cancer prevention behaviors.

Conclusion: Future studies that examine how genetic counselors effectively aid their patients in the consideration of prevention options will become increasingly important as additional low-penetrance genes are identified, increasing the number of patients to whom genetic testing will be relevant.

How to Use Surveillance Data for Cancer Research

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Purpose: Disease surveillance—the monitoring of characteristics of interest in defined populations over time—provides communities, countries, and regions of the world with important tools for public health action. Many countries have long standing and well established cancer surveillance programs, and even in low resource countries, high quality cancer registration systems and cancer surveillance are becoming more possible. Surveillance is a cornerstone of cancer control planning and evaluation, but also plays an important role in cancer control research.

Methods: Surveillance data can be used for evaluating the effectiveness of cancer control activities at the population level, such as changes in individual risk behaviors (sun protection, tobacco use, etc), implementation of screening or treatment programs, or changes in health care delivery and cancer treatment. Environmental risks at the local or regional level are often first identified through analysis of surveillance data. With the increased use of new computer-based methodologies for analysis of geographically referenced data, such as GIS, it has become possible to link surveillance data to many other types of public and commercial data, allowing researchers to explore relationships at the ecological level between features of the physical and social environment and cancer outcomes.

This talk will review some of the newer methodologies for analysis of surveillance data, including types of research questions and possible data sources for addressing those questions, statistical analysis issues and methods, and issues of confidentiality in data use and dissemination of results. Examples of current research in cancer control using surveillance data will be presented.

Experience of On-Line Registration of Breast Cancer in Korea

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Purpose: Korean Breast Cancer Society (KBCS) was originated from the Korean Breast Cancer Study Group made by some breast surgeons in 1991, progressed to the Society in 1996. For the first project, KBCS collected the nationwide data by means of the off-line questionnaire.

Methods: In 2001, We developed the on-line registration system to solve the problems of time-consuming in data collection and the quality of data. There are two sets of data in registration — one is essential, and the other in optional. By using this system, anyone can get their own data or collective data of KBCS whenever, whatever, wherever they want.

Results: Now, there are more than 50,000 data base of Korean breast cancer patients including 8,500 cases of mine, and more than 100 university, general hospitals and private clinics are attending this system. The registration rate of 2002 is 69.5% (5455/7845) and that of 2004 is 71.1% (6878/9667). From 2003, KBCS has collaborated with the Korean Central Cancer Registry (KCCR) to get the Korean breast cancer 10-year survival data of 1993-2002. In 2006, KBCS completed this project and published the data of overall, relative period, breast-cancer-specific survival rates according to the age, sex stage, lymph node status, hormonal receptor status and others.

Conclusion: We will discuss the background of the initiation of this program, current status of the Korean Breast Cancer Data, short-time program demonstration, privacy law in Korea, survival data of Korean Breast Cancer patients.

Use of Community Based Participatory Research in Breast Cancer Prevention and Control

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Introduction: Community Based Participatory Research (CBPR) is collaboration between community groups and researchers for the purpose of creating new knowledge or furthering understanding about an issue to bring about change. The issue is generated, ideally, by the community and its members participate in all aspects of the research process. The process is guided by a series of principles for collaboration, participation, empowerment, and is systematic and transformative. CBPR is becoming increasingly important as communities are being required to take greater ownership and control over decisions affecting the health of the individuals in the communities. It is also gaining a strong presence in the area of breast cancer control.

Session Objectives: The session objectives include the following: 1) Defining CBPR as a methodological approach to breast cancer control interventions; 2) Presenting key principles of the CBPR approach; and 3) Describing the process of establishing.

Presentation Format: The interactive presentation will review the principles of CBPR and illustrate application of its use in a study of breast cancer screening with U.S. faith-based organizations. Other examples in the literature of uses of CBPR with breast cancer control interventions will also be highlighted.

Conclusion: The goal of the presentation is to enable Korean health care providers and community and advocacy-oriented organizations to gain an understanding of the usefulness of CBPR in promoting breast cancer control in both urban and rural community settings. The presentation will be interactive and input from the participants is welcomed and expected.

Empowerment and Participatory-based Education Materials

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Objective: The purpose of this presentation is to introduce a participatory learning model and community-produced material for breast cancer education.

Background: Health education is grounded philosophically in the model of a partnership between the client and the professional in which each partner share the responsibility and initiative. Health educators have adopted a central theoretical framework in which learning is conceived to be a process of participation and collaboration that is prompted by the learner's lifelong drive for understanding and personal growth. In learning, participation may be viewed not only as an efficacious method of transferring knowledge, but also as a process by which the learner, by becoming involved, gains confidence in solving his or her problems. Most educational efforts in the past have concentrated on effecting changes in people's knowledge under the assumption that increased knowledge would change behavior. However, in recent years emphasis has shifted away from strategies designed to change knowledge to experiential education activities that are learners directed. One participatory learning model is a photonovel which is a booklet similar to an American comic book, but photographs of real people and real places replaces the cartoons; the dialog is presented in word bubbles, as in comic books.

Methods: The team of Korean American Cancer Project in Maryland developed a photonovel for breast cancer education in response to the lack of culturally relevant cancer education material. The work group for developing the photonovel was recruited from Korean American communities and the group served as a guide in specifying and refining the contents and formats of photonovel. Every effort was made to follow the critical principles of participatory research, which emphasized mutuality and partnership between researchers and the target community. Specifically, the work group determined (1) the cultural relevance, (2) literacy, and (3) acculturation congruence of the photonovel. In addition, all the members of the work group participated in designing the cover, photography, assembly and layout of the photonovel, pre-testing, and evaluation.

Results: As process evaluation, a month after the pretest and intervention program with distribution of the photonovels, the study team conducted a mailed survey first and then a telephone survey for those who did not respond to the mailed survey. The survey asked them of their opinions on the photonovel. Of the 120 women in the intervention, 109

(91%) responded to a one-page questionnaire, 78% returned the questionnaire by mail and the remaining 22% who did not return the questionnaire by mail completed telephone survey. The overall evaluation of photonovel was very positive: 92.7% read the photonovels. Among those who read them, about 93% agreed that photonovels were very helpful or helpful in learning about the importance of breast cancer screening; half of women recommended them to their family, relatives, and friends.

Conclusion: A participatory learning approach has been successfully implemented to increase the acceptability of the breast cancer educational messages in Korean Americans who is one of hard-to-reach population groups. The investment of health education efforts in community-empowered activities may be an important step in coming to terms with victim blaming which fosters a sense of individual responsibility and reaction to socially induced, health-threatening conditions, rather than a more effective and political collective responsiveness. Moreover, through such activities, health education can fulfill its people-enhancing and people serving potential.

Neoadjuvant Chemotherapy for Operable Breast Cancer

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Primary chemotherapy has been a standard therapeutic modality for locally advanced breast cancer for sometime. It has been well documented that both neoadjuvant and adjuvant chemotherapy are equally effective in disease free survival (DFS) and overall survival (OS), when the same chemotherapeutic agents are used. NSABP B-18 data as well as other randomized trials supported this. Primary chemotherapy could result in increased breast conserving rates and determining the good prognostic patients by a surrogate marker-pathologic complete response (pCR). It takes shorter time to assess the efficacies of new drugs and biological agents compared with adjuvant trial outcomes that it has become a useful tool to develop adequate adjuvant therapy. More recently anthracyclines in combination or sequentially with taxanes have shown clearly superior efficacies including pCR, DFS and OS. Currently there are several ongoing trials incorporating capecitabine in combination with anthracycline/taxane or sequentially with anthracycline/taxane regimens. One of such phase III studies randomizing docetaxel/capecitabine (TX) versus doxorubicin/cyclophosphamide (AC) performed at NCC Korea showed that superior efficacies by TX with increased pathologic and clinical complete response rates. The patients who achieved pCR in LN developed significantly less recurrence. Although the use of primary chemotherapy has been expanding to the earlier stages of breast cancer, more questions have to be answered. Clinical investigators in Korea in collaboration with Japanese Breast Cancer investigators are going to embark on a new clinical trial assessing primary chemotherapy followed by further adjuvant chemotherapy depending on the residual disease to answer one of those semantic questions.

Adjuvant Trastuzumab; Timing, Duration, Management of Toxicity

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Trastuzumab (Herceptin) is a humanized, monoclonal antibody to the Her2 neu receptor which is over-expressed in approximately 15 to 20% of patients with breast cancer. The presence of this growth factor gene over-expression is associated with more aggressive disease. The pivotal trials in metastatic breast cancer in the late 1990's demonstrated that trastuzumab combined with chemotherapy produced significantly higher response rates, improved time to progression and superior overall survival compared to chemotherapy alone. There have been five clinical trials conducted to evaluate the effectiveness of Herceptin when used in combination with chemotherapy in women with early breast cancer. In the four large trials, more than 13,000 women were randomly assigned to either standard chemotherapy alone or the same chemotherapy plus Herceptin for one or two years. A small Finnish trial of 232 women, evaluated 9 weeks of Herceptin given with a on-standard chemotherapy regimen. Each trial confirmed a statistically improved disease-free survival with a 42% to 50% reduction in the risk of relapse. In the four larger trials, a statistically significant overall survival benefit with a 33% to 41% reduction in the risk of death was seen. The only significant side effect associated with the inclusion of Herceptin was a higher incidence of cardiac dysfunction. This ranged from 1.7% to 4.1% in those patients receiving Herceptin, compared to <1% in the control group. In the context of the current adjuvant trial results, the use of adjuvant trastuzumab will be discussed.

Update on Systemic Therapy for Women with Metastatic Disease

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Over the last decades, improvements in systemic therapy and introduction of several new agents into clinical practice have significantly improved disease control and obtained some survival benefits in early-stage and metastatic breast cancer. Important improvements have been achieved in endocrine treatment. Among them, aromatase inhibitors have proved to be superior to standard endocrine therapies in either first- or second-line treatment in women with postmenopausal, metastatic breast cancer and a novel antiestrogen compound, fulvestrant, has been introduced in clinical practice. Chemotherapy remains the treatment of choice for endocrine unresponsive or refractory breast cancer patients. Anthracyclines and taxanes have a great impact on the treatment of breast cancer and several other cytotoxic chemotherapeutic agents have been considerably useful in the control of metastatic breast cancer. With a greater understanding of the molecular biology of breast cancer, targeted agents that disrupt specific cellular targets and signaling pathways have been incorporated into routine clinical practice. And the development of better predictive and prognostic markers enables clinicians to select better patients who could benefit from such therapies. For example, in the subgroup of patients with tumors that overexpress HER-2, the use of targeted agents that disrupt HER-2 signaling has modified the natural history of HER-2 overexpressing breast cancer. We will discuss about some of landmark achievements over last 2 decades and the currently available treatment options for patients with metastatic breast cancer.

Emerging Targeted Agents for Breast Cancer Treatment

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The desire to provide less toxic and more effective therapeutics for cancer patients has led to the exploration of novel therapies. Targeted therapies represent a new generation of drugs that interfere with specific molecular targets having critical roles to play in tumor growth or progression. The principle of targeted therapy is not new: tamoxifen, targeted at the ER, has been in use for more than 30 years. Major breakthroughs in our understanding of cancer biology have permitted us to make initial steps into the arena of 'targeted therapies'. Trastuzumab, a humanized monoclonal antibody to HER2/neu, is the first molecular targeting agent approved for therapy of MBC, capable to significantly improve clinical outcome in combination with cytotoxic therapy. Recent data from randomized, prospective, clinical trials suggest that trastuzumab decreases the risk of early recurrence by 50% in patients with HER2-positive disease. Lapatinib is an orally active dual HER2/neu and the EGFR (c-erbB-1) inhibitor. Lapatinib is effective as a single agent and in combination with capecitabine, for the treatment of HER2-overexpressing MBC who received prior therapy with an anthracycline, a taxane, and trastuzumab. Lapatinib penetrate the central nervous system and be effective against brain metastases. Other novel targeted treatments are in clinical evaluation, including antiangiogenic compounds [Bevacizumab, PTK787 (Vatalanib) and ZD6474 (Vandetanib)], small molecule multitargeted TK inhibitor (Sunitinib, Sorafenib, Pazopanib), mTOR inhibitor [Temsirolimus, (CCI 779) Everolimus (RAD 001)], HER inhibitor (Canertinib, BIBW 2669, BIBW 2992, HKI-272, Pertuzumab), PARP inhibitor showing promising activity. This lecture provides an updated overview of targeted therapy in breast cancer.

Micrometastasis in SLN; Clinical and Pathological Significance

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Purpose: Sentinel lymph node (SLN) biopsy has been established as a standard procedure in the treatment of patients with early breast cancer. The introduction of intra-operative cytokeratin (CK) immunohistochemistry (IHC) on frozen sections has resulted in the improvement of the micrometastasis detection rate. Currently, micrometastasis has been defined and subclassified into micrometastasis or isolated tumor cells (ITC), according to the size of the lesion in the 6th edition of the AJCC TNM classification system. However, the clinical implication of micrometastases in SLN is still unclear.

Methods: SLN biopsies were performed in 410 patients from Nov. 1998 through June 2004 at the Breast Cancer Center of Yong Dong Severance Hospital.

Results: 134 patients (32.7%) showed metastases, among whom 29 (23.4%) had micrometastases. The sizes of the metastatic deposits were less than 0.2 mm in 23 patients (79.3%), and between 0.2 mm and 2 mm in 6 patients (20.7%). Tumor cells were not identified on H&E sections of SLN, but were detected on CK IHC in 16 patients (55.2%). Metastatic tumor cells were located in the subcapsular sinus in 8 patients (27.6%), both in the sinus and parenchyma in 12 patients (41.4%), and only in the parenchyma in 9 patients (31.0%). Non-SLN involvement in patients with SLN micrometastasis were observed in only two patients (9.2%) with primary tumors of 3.0 cm and 3.2 cm in size.

Conclusion: Axillary lymph node dissection is not warranted in those patients with a tumor size of less than 2 mm in diameter, and it is mandatory to use CK IHC in order to improve the diagnostic accuracy of SLN micrometastasis.

Biological Evaluation and Strategy for Triple Negative Breast Cancer

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Purpose: Triple negative (TN) breast cancers are characterized by the lack of expression of estrogen receptor (ER) and progesterone receptor (PgR), and the absence of HER2 protein overexpression, and so there is still no targeted therapy for this subtype. In this study, we examined the biological and prognostic characteristics of TN breast cancer.

Methods: Between January 1998 and December 2006, 1,663 patients with primary breast cancer were included in this study and the ER, PgR and HER2 status were evaluated in all cases. Out of the 1,663 patients, 156 were treated with neoadjuvant chemotherapy (EC, ET or FEC-DOC regimen).

Results: Patient distribution according to the ER, PgR and HER2 status was as follows; ER and PgR positive: 58.5%, ER and PgR negative: 25.1%, and TN: 13.7%. TN breast cancers had high proliferation rates, high nuclear grade, and frequent p53 overexpression. HER2 positive reflected a high grade of malignancy in endocrine responsive tumors, whereas HER2 negative correlated with a high proliferation rate in endocrine non-responsive tumors. With regard to neoadjuvant chemotherapy, the response rate to chemotherapy was significantly higher in TN cancer. However, patients with TN tumors had a significantly poorer disease-free survival (DFS) and an overall survival (OS) rate after recurrence than those with non-TN tumors.

Conclusion: TN breast cancers are a rare subtype and have high proliferation rates, high nuclear grade, and p53 overexpression. TN breast cancer is a chemosensitive subtype, but has a lower DFS/OS. To improve the prognosis of TN breast cancer, a new effective strategy needs to be developed.

HER-2 Standardization Program in Korea

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Purpose: Accurate evaluation of HER-2/neu contributes to an increase in survival rates. IHC can be easily accessed in most of labs at minimal expense, but it has drawbacks of inconsistency and lower accuracy due to the fixation status of tissue, different specificities of antibodies and interdepartmental variability. The importance of quality control of IHC and reproducible evaluation of HER-2/neu protein over expression must be emphasized in order to improve survival rates of breast cancer patients.

Methods: Five unstained slides from paraffin blocks of breast cancer with IHC results of 0, 1+, and 3+ were distributed to laboratories. After IHC on their own, the pathologist in each lab recorded and compared his/her results with the already established results. Afterwards, the pathologists simultaneously reviewed the slides once again in one place.

Results: A total of 23 laboratories participated. The concordance rates of IHC results were 86% for A(3+), 82% for B(3+), 41% for C(1+), 76% for D(0), and 61% for E(0).

Conclusion: The concordance rates of IHC results for 3+ were relatively high in comparison to that for 1+. With reference to several published articles, FISH is usually recommended only for cases showing equivocal results on IHC. However, under the circumstances in Korea, confirmation of HER-2/neu status by FISH is essential in every breast cancer patient in order to select appropriate candidates for trastuzumab (Herceptin®) treatment, unless standardization and quality control of IHC is well-established.

Third Generation Adjuvant Chemotherapy - Increasing Efficacy, Minimising Toxicity

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Third generation, taxane based combinations including TAC, FEC x 3 followed by T, and dose dense chemotherapy regimes offer additional efficacy in terms of improvement in mortality and risk of relapse at the cost of increased risk of toxicity, in particular myelosuppression. Their safe administration requires careful patient selection, patient education, meticulous attention to monitoring of toxicities and preventative strategies including growth factor support and/or prophylactic antibiotics. Risk of febrile neutropenia remains the most concerning potential acute toxicity of chemotherapy which can be effectively prevented by primary prophylaxis with growth factor support with or without antibiotics prophylaxis. This presentation will review the rationale for the currently used third generation adjuvant chemotherapy regimes with particular emphasis on safety and toxicity issues, including prevention and management of bone marrow suppression and risk of infection but also other less common toxicities including hypersensitivity, neuropathy and fluid retention.

Mammography and Ultrasound Findings of Breast Cancer

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Mammographic evaluation is a two step process: first step is perception, and second step is interpretation. The majority of invasive breast cancers is stellate and is usually easily perceived on mammograms. 93% of all stellate lesions are malignant. Distribution, morphology and density are essential characteristics to differentiate microcalcifications associated with benign and malignant diseases. Calcifications are easy to perceive, regardless of the parenchymal pattern. However, many benign and malignant calcifications share common characteristics that make their differentiation difficult or impossible. 80% of all calcifications are benign, and core needle biopsy helps avoiding many surgical biopsies. Circular/oval shaped lesions are usually easily perceived on mammograms, and as with calcifications, the majority of them are benign. US is the primary modality to supplement mammography. Preoperative US is useful in defining the local extent of disease. Color/power Doppler helps in further differentiation, in delineation of extension, and in following response to chemotherapy. Whole breast US screening is effective in detecting early stage cancers in asymptomatic women with mammographically normal dense breasts. Unnecessary biopsies from US screening can be prevented when characterization criteria are strictly applied in BI-RADS 3 lesions. Speckle reduction (SRI), compound (CUS) and tissue harmonic (THUS) imaging are new sonographic technologies with advantages over fundamental sonography. In the evaluation of solid breast masses, SRI and CUS are the most beneficial. US elastography is based on assessment of differences in stiffness of tissues, and is valuable in increasing the diagnostic specificity. Its impact is significantly more evident in lesions smaller than 1 cm.

Roles of MRI in Breast Cancer Treatment and Research

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The role of MR imaging in breast cancer is valuable as an adjunct in the diagnostic evaluation of mammographic findings or clinical examination. To review of breast MRI in breast cancer with use, performance and treatment is purposed. Indications for breast MRI as follows; 1) preoperative staging with exact tumor size, associated malignancy, multicentricity, involvement of skin, pectoralis muscle, or chest wall, contralateral breast, locoregional lymph node, and distant metastasis, 2) monitoring neo-adjuvant chemotherapy response, 3) assessment of residual disease after lumpectomy and positive margin, 4) local recurrence detection after breast conserving surgery or in the chest wall after mastectomy, 5) positive axillary lymph node with unknown primary, 6) indeterminate mammographic or ultrasonographic findings, 7) evaluation of augmented breast, and 8) screening of high risk group. Accurate assessment of response in treatment by diffusion-weighted image or spectroscopy is valuable.

Breast MRI in breast cancer has an important roles in pretherapeutic and posttherapeutic assessment. Functional measurements in breast MR promise great sensitivity for detecting biologic effects of targeted treatment.

Roles of PET/PET - CT in Breast Cancer Treatment and Research

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Positron Emission Tomography (PET) is a functional imaging modality that uses positron-emitting radioisotopes to non-invasively image various biological processes. Positron is generated from the nucleus when a proton changes into a neutron. It is exactly the same as electron, except that it has positive charge. These positrons will react with surrounding electrons after leaving the nucleus, a process called annihilation reaction, which will convert the particles into gamma energy. When the energy leaves (Emission) the patient's body, special detectors will collect and create 3-dimensional images.

Currently, the most widely used positron emitting tracer is F-18 FDG (Fluorodeoxyglucose). This tracer is an analogue of glucose, which will then be taken up into the cell by a cellular membrane transporter. However, unlike glucose, F-18 FDG will not be further metabolized after a certain step, effectively being trapped within the cell as a metabolic intermediate, allowing images to be taken after some period of time. FDG is a currently in the spotlight as an excellent tracer, especially in the oncology field, because of its ability to detect metabolic changes within malignant tumors. The theoretical basis for this process was presented by Warburg in the 1930s, who reported that malignant tumors have higher rates of glucose metabolism compared to normal cells.

Breast cancer is one of the most common tumors in women. Mammography is an important screening modality in the detection of early breast cancer. It has high sensitivity but low specificity. Ultrasonography is more specific and with ultrasonography guided biopsy, provides more diagnostic information. Recently, magnetic resonance imaging is actively being used, but it is not tumor specific. Ever since 1989, after minn and soini imaged breast cancer with FDG, PET has been investigated on its use for early diagnosis of primary breast cancer, differentiation between benign and malignant diseases, staging, assessment of therapeutic effect, and detection of recurrence.

FDG PET for early diagnosis of breast cancer has some limitations. The current resolution limit for most PET scanners is about 5 mm, so the metabolism for tumors smaller than 1 cm can be underestimated, and with regard to pathology, lobular carcinomas have lower FDG uptake compared to infiltrating ductal carcinomas, which can be a cause for high false negative rate. FDG PET may not have a prominent role in multicentric tumors as well. According to one meta-analysis, even when FDG PET was negative in patients with abnormal findings on mammography or physical examination, there was

a 12.1% of false negative rate. Therefore, based on the current results, the role of FDG PET in reducing invasive studies in benign looking tumors is not definite. Recently, more dedicated PET device for breast imaging such as positron emission mammography (PEM) has been developed to improve spatial resolution of PET and early studies have suggested promising results. Unlike the limited sensitivity, the specificity of FDG PET has been approximately 90% in most studies.

Axillary LN metastasis is one of the most important prognostic factors in breast cancer, but accurate staging is difficult using anatomical imaging. The usefulness of FDG PET in axillary LN metastasis shows that larger primary tumors have higher accuracy for the detection of axillary LN metastasis. In general, specificity and sensitivity of PET tends to show an inverse proportion, within the ranges of 80–100%. The advantage of LN evaluation with FDG PET is the detection of metastasis to extra-axillary LNs such as supraclavicular, mediastinal, or internal mammary chain. The detection of extra-axillary LN metastases would change tumor staging and significantly alter treatment plan. However, microscopic metastasis can be still better detected by sentinel lymph node sampling. Therefore, FDG PET and sentinel lymph node sampling should complement each other so that comprehensive evaluation of axillary lymph node metastasis can be performed.

Traditionally, chest x-ray and CT were taken to evaluate for lung metastasis, ultrasonography, CT, or MRI for liver metastasis, and whole body bone scintigraphy for skeletal metastasis. Instead of going through all of these studies, FDG PET can evaluate distant metastasis regardless of locations in one examination. Considering the reported sensitivity and specificity of FDG PET ranging from 80 to 97% and 75 to 94%, respectively, the value of FDG PET for distant metastasis seems at least comparable to other conventional imaging. In cases of skeletal metastasis, the sensitivity of FDG PET can be different for osteoblastic or osteolytic lesions, with FDG uptake being lower for osteoblastic metastasis. Osteoblastic metastatic foci can be small so it might be invisible on FDG PET, but because these foci can cause severe reactive bone changes, whole body bone scintigraphy can be more sensitive.

When preoperative neoadjuvant chemotherapy is performed, the evaluation of treatment response is important in prediction of the patient's survival. With size criteria, the evaluation of treatment response seems very difficult in the early stage of therapy. The differentiation between residual tumor and treatment related change is quite challenging as well. In contrast, the alteration of glucose metabolism can effectively detect therapeutic response as early as the first cycle of chemotherapy. If the metabolism is not decreasing after starting chemotherapy, it may predict a poor response to chemotherapy. Further studies should be performed to decide the ideal period of time to conduct FDG

PET for response evaluation. Other than evaluating response to neoadjuvant chemotherapy, FDG PET is also useful for monitoring treatment response in patients with metastatic breast cancer.

In addition to the above mentioned clinical applications, the increased tumor metabolism on FDG PET can be compared with the status of hormone receptors, histologic grades, or expression of certain proteins like p53, and may serve as an a surrogate making tumor characterization possible without necessarily retrieving tissue specimen. A few radiotracers other than FDG are being applied in breast cancer such as radiolabeled estrogen or tamoxifen with promising preliminary results.

Monitoring of Cell Therapy with MR Imaging

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In molecular imaging science, MR imaging has emerged as a leading technique because it can provide high-resolution three-dimension maps of the living subject. The two major classes of MR contrast agents are paramagnetic contrast agents, usually based on chelates of gadolinium generating T1 positive signal enhancement, and super-paramagnetic contrast agents that use mono- or polycrystalline iron oxide to generate strong T2 negative contrast in MR images. These paramagnetic or super-paramagnetic complexes are used to develop new contrast agents that can target the specific molecular marker of the cells or can be activated to report on the physiological status or metabolic activity of biological systems. Various enzyme systems (e.g. Tyrosinase, β -galactosidase, peroxidase) or internalizing cell receptors have been exploited for the detection gene expression by MR imaging.

Despite recent advances in cancer research techniques, we are still limited in our ability to detect tumors in their earliest stage of formation, monitor tumor phenotype, quantify invasion or metastasis, or visualize the real-time in vivo activity of anticancer therapeutics. Techniques such as magnetic resonance (MR) imaging and optical imaging are likely to revolutionize the way we detect and monitor cancer over the next decade. These technologies, coupled with recently developed molecular probes designed to recognize tumor-specific markers, can already be used to visualize and quantify tumor growth or regression during therapy.

SLN Biopsy Technique; Is There the Best One?

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Purpose: The standard of care in the management of the axilla for a woman with breast cancer had been a level I and II axillary lymph node dissection (ALND). The sentinel lymph node biopsy (SLNB) in breast carcinoma has come to replace ALND in women with clinically negative axillas. With the increased use of SLNB, the best method of identification of the SLN is yet to be determined.

Methods: The majority of surgeons in the U.S. and around the world use a combination of blue dye (lymphazurin, patent blue or isosulfan) and technetium labeled sulfur colloid. While others use technetium labeled antimony trisulfide, methylene blue or indocyanine green. There is also debate on the site of injection with intradermal, subdermal, peritumoral and intratumoral have all been reported.

Results: Across the published studies, the mean false negative rate is under 10%, with the larger studies having a lower rate. The success of mapping across most large studies is over 95%. The average number of lymph nodes harvested averages 2. The reported success of mapping in general is improved with both blue dye and radiocolloid as opposed to single tracer method, while in experienced hands single tracer method shows a high degree of success.

Conclusion: The best method of identifying a sentinel lymph node in breast cancer has yet to be determined. Most surgeons benefit from the combination of radioisotope and blue dye in achieving high identification rates and low false negative rates. In experienced hands a single tracer method of identification can be very successful.

The Current Status of SLN Biopsy of Breast Cancer in China

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Purpose: China Multicenter Study of Sentinel Node Biopsy (SNB) Substituting Axillary Node Dissection (AND) in Breast Cancer was conducted from Jan. 2002, with about 2,000 SNB patients recruitment this June. The primary objectives were 5ys DFS and complications between SNB and AND. The second objectives included 5ys OS, SLN intraoperative diagnosis, Micrometastasis detection and prognosis, and radiologic safety.

Methods: Combined methylene blue dye and 99mTc-sulfur colloid or 99mTc-IT-Rituximab were used for SNB. Based on 1,752 SNB cases available before Apr. 2007, the median age was 47ys. Biopsy type included core biopsy 1,126 cases, open biopsy 456, and intraoperative biopsy 170. Tumor size was less than 5 cm in 98.8% patients. The median number of SLN was 2. The type of surgery was BCS+SNB 50.6%, Mastectomy+SNB 27.4%, BCS+AND 8.7%, and Mastectomy+AND 13.3%.

Results: According to our study, preoperative lymphoscintigraphy was by no means a MUST. The FNR of SLN intraoperative with frozen section and touch imprint cytology combination was less than 5%, could make most SLN positive patients with ALND in one operation. SNB was radiologically safe for both patients and surgeons (2,000 cases SNB per year). Serial section H&E increased macro-/ micro-metastasis detection in 18.4% cases and 9.0% SLNs. The optimal interval was 300 μ m in our study. Serial section IHC could further increase macro-/micro-met. Detection (8.2% cases). With a median F/U of 42 months in one early center, two cases of axillary relapse (0.82%) were found in 244 SNB cases, while the complications of SNB were significantly lower than that of AND.

Safety Margins for Lumpectomy; How Close is Too Close?

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Breast conserving surgery (BCS) is not inferior to mastectomy in survival; the risk of BCS is local recurrence (LR).

LR rate after BCS at 6 to 20 years ranged from 7% to 19%, but the LR after mastectomy developed in 2% to 14%. Kurtz et al. reported that the actuarial incidence of LR increased from 7% at 5 years to 14% at 10 years and 20% at 20 years after treatment, but the most LR after mastectomy occur within the first 3 years after surgery.

LR has been classified by the location in relation to the original tumor such as true recurrence (within the boosted region), marginal miss (adjacent to the boosted region) and new primary (at a distance from the original tumor).

Gage et al. reported on 1,628 patients with stage I or II invasive carcinoma with BCS and radiotherapy, the annual incidence rate for a true recurrence/marginal miss recurrence was between 1.3% and 1.8% for years two through seven after treatment and then decreased to 0.4% by 10 years after treatment. In contrast, annual incidence rate for recurrence elsewhere in the breast increased slowly to a rate of approximately 0.7%/years at 8 years and remained stable.

Veronesi et al. noted that the median time to true recurrence was 92 months compared with 119 months for cancers occurring elsewhere in the preserved breast.

In the largest group of study, negative margins are not defined quantitatively, however status of resection margin are classified such as positive margin (PM), negative margin (NM; 1 mm, 2 mm, 3 mm and so on) and close margin (CM; between cut edge and negative).

Singletary reviewed 34 published reports about clinical significance of marginal status and risk factors for PM. LR was increased in case of PM compared to NM. The largest group of studies used >2 mm as the cut-off for negative margin.

The adverse affect of PM on LR increased with increasing follow up times, however for NM, there was no significant change in LR rate at follow up times ranging from 36-120 months.

There was no clear cut difference based on margin width. The LR rates in patients with a 1mm NM shows 0% to 7% (median 3%) while the LR rates in patients with a 2 mm

NM shows 3 to 10% (median 6%) and patient with microscopic NM show LR rates between 2% and 4% (median 2%). In our study, we follow up 37.2 months after BCT and RT in 348 patients with stage I and II.

The LR rates for patients with a CM (<1 mm) and NM (>1 mm), were 6.7% and 3.5%, there was no statistical difference.

Singletary also reviewed 10 studies in which LR associated with negative, close and positive margins were recorded. In 3 of 10 studies, the LR rate for CM are similar to NM, in 4 studies they are intermediate between NM and PM, and in 2 studies LR rates for CM are similar to PM.

DCIS has some special problems in BCS.

Holland has demonstrated that there is frequent microscopic tumor at more than 20 mm from one apparent edge of DCIS. Because of the tendency of DCIS to be multifocal and skip lesions, it may be difficult to determine if a margin is negative really signifies complete excision of the DCIS. So NM as large as 5 mm (Vicini et al) and even 10 to 15 mm (Silverstein et al) have been suggested

Singletary summarized 7 studies about LR rate according to the marginal status in patients with DCIS treated with BCS. As with IDC, there is significant higher LR rate seen with PM compared with NM. Interestingly, although the NM used in the majority of these studies were equivalent to those used with IDC (1 to 2 mm), the LR rates in these studies were not significantly higher than those seen in the studies of IDC.

The study by Silverstein et al. reported an unusually high LR rates associated with NM defined as greater than 1 mm (LR rate = 15%) but if the NM was defined as 10 mm or more the LR rate was only 3%.

In addition to surgical margin status, young age, large tumor size, lymphovascular invasion, EIC, positive lymph nodes, not receiving adjuvant therapy, lobular or ductal extension were also important.

Preoperative methods are inadequate, histological evaluation is essential. In order to determining completeness of excision, different techniques are used; minimum width of the margin, cavity shaving, intraoperative cytology and frozen biopsy.

Because of the wide range of confounding factors, it is still not clear whether obtaining a safety margin during BCS. The wider excision gives poor cosmetic results but gives lower LR rates. But base on the above, smaller margin is feasible in both IDC and DCIS.

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Breast Conserving Treatment in Japan: Long-term Follow-up Results and Issues to be Addressed

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Purpose: Approximately 60% of patients with breast cancer are treated with breast-conserving treatment (BCT) in Japan at present. Long-term follow-up results of BCT for early stage breast cancer at our institution were evaluated. Risk factors of ipsilateral breast tumor recurrence (IBTR) were also investigated.

Methods: Long-term follow-up results of BCT with or without radiation therapy were evaluated, stratified by the operation period; earlier (1986-1990; n=61), middle (1991-1994; n=229), and later (1995-1990; n=656). Overall survival, distant disease free survival and IBTR rates were calculated by the Kaplan-Meier method. Risk factors for IBTR were examined by multivariate analysis using the Cox proportional hazard model.

Results: The 10-year overall and distant disease free survival rates were favorable, and 10-year IBTR rate was less than 10% as a whole. Despite the expansion of indication of BCT, local control rates improved. The 5-year incidences of IBTR were 8.0% in the earlier, 7.2% in the middle and 3.4% in the later period, respectively ($p < 0.05$). Multivariate analysis showed that young age, positive margins and omissions of radiation therapy as well as omission of adjuvant endocrine therapy were significant risk factors of IBTR.

Conclusion: The IBTR rate appears to be declining probably due to appropriate administration of radiation therapy and increased use of adjuvant systemic therapy. The risk factors identified were similar to the results of the collaborative study group conducted with the support of the Japanese Ministry of Health, Labour and Welfare (Komoike Y et al. *Cancer* 106:35, 2006).

Measurement of HRQOL in Korean Breast Cancer Patients

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Health related quality of life (HRQOL) in Korean patients with cancer had been rarely studied, mostly due to the lack of a culturally and psychometrically validated cancer-specific QOL instrument. Commonly used cancer specific QOL instruments, such as FACT-G and EORTC QLQ-C30 in the U.S.A. and Europe, has been reported to be partially cultural differences in the application for Korean breast cancer patients. Therefore, cancer specific QOL (C-QOL) has been recently developed Korean patients with cancer. The C-QOL consists of 21 items with a 5-point Likert-type scale, included five sub-domains: physical status (6 items), emotional status (6 items), social function (3 items), concerns (2 items), and coping function (4 items). The items of C-QOL was derived from a qualitative study using the grounded theory and established content validity, construct validity, convergent validity, discriminant validity, known-groups validity, reliability, and sensitivity. The reliable and valid C-QOL can be used in practice and for a study with Korean breast patients with cancer. However, the C-QOL is a paper-and-pencil type of questionnaire. This type of questionnaire has some limitations, which is difficult to use in busy oncology practice and costs personnel expenses and time in scoring the obtained data. One of the solutions may be the change of the paper-and-pencil C-QOL into computerized C-QOL. Thus, touch screen computerized C-QOL was developed and evaluated.

The Meaning of Prayer in Patient with Breast Cancer

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Purpose: Spirituality in cancer patient is an expression of spirit which is entity of human being, having dynamic process strengthened in suffering due to struggle with cancer and unique characteristics according to the individual's religion, age, past experiences and burden of family. Prayer is a spiritual practice and a religious practice and highly valued by those who use it. Prayer is a significant coping strategy employed by the patients to find comfort, decrease anxiety, and facilitate hope and peace. Yet no research has explored the lived experience of using prayer to cope with illness. Specific purposes are 1. obtain descriptions of cancer patients' from semi-structured interviews, 2. analyze and present these descriptions, 3. identify why, when and how patients pray and what they pray about and the outcomes expected and 4. provide nursing implication.

Methods: It is an exploratory and descriptive study.

- Sample
 - 1) Participants included 15 adults living with or surviving breast cancer.
 - 2) Various religious backgrounds are included.
 - 3) IRB was approved.
- Procedure
 - 1) Participants were recruited from nurse, clergy and physicians.
 - 2) Data was collected during audiotape-recorded semi-structured interview.
 - 3) Interview took place in researcher's office, head nurse's room and patient's home.
- Analysis

Each taped interview was transcribed verbatim, initially each transcribed interview was read. Two researchers to become intimate with thoughts and feelings of the informants. Significant statements were underlined for extraction for the theme. Two researchers compared the data to identify the salient and recurrent themes and compared them across participants to better understanding their meaning.

Subgroups of Women with Breast Cancer with Different Symptom Experiences and Outcomes: A Cluster Analysis

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Purpose: To identify subgroups of women who are receiving initial chemotherapy +/- radiation therapy based on their experiences with the symptoms of fatigue, sleep disturbance, depression, and pain. To describe whether patients in the subgroups differed on functional status and quality of life and membership changes for the individual during and after cancer treatment.

Methods: A large randomized clinical trial testing the effect of an exercise intervention on cancer-related fatigue and associated symptoms. 112 patients completed a demographic questionnaire, Karnofsky Performance Status scale, Piper Fatigue Scale, General Sleep Disturbance Scale, Center for Epidemiological Studies - Depression Scale, Quality of Life Scale - Cancer, and worst pain intensity question at the initiation of chemotherapy (T1), at the end of treatment (T2), and at the end of the study (T3). A cluster analysis was used to identify patient subgroups based on patients' symptom experiences.

Results: At T1 and T2, four relatively distinct subgroups were identified. At each time point, the High intensity symptoms group (HS) showed the lowest QOL mean score. HS group also showed the lowest functional status at T2 and T3. There were subgroup membership changes for the individual over the course of treatment, and recovery periods. At T3, all patients had at least a mild experience of one of four selected symptoms.

Conclusion: Clinicians need to assess patients for the occurrence of multiple symptoms that may place them at increased risk for poorer outcomes. Future considerations include measurement of multiple symptoms and characteristics of changing cluster group memberships over the course of the cancer treatment.

Coping of Chinese Women with Breast Cancer

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Purpose: A cancer diagnosis imposes demands on every aspect of a patient's life. Cultural factors play a significant role in influencing patients' coping and available resources. Since few studies have examined the coping of Chinese patients with cancer, a two-staged grounded theory study was conducted to understand the phenomenon of coping after Chinese women are diagnosed with primary breast cancer and to identify conditions explaining differences in coping outcome.

Methods: In the first stage, using a broad interview guide developed by the researchers, cross-sectional interviews were conducted with fifteen women at different stages of the cancer experience (3 were newly diagnosed, 6 were receiving treatment, and 6 had completed treatment). In the second stage, longitudinal interviews were conducted when the women were newly diagnosed, receiving treatment and at 3 months after treatment completion. Nine women were interviewed at the beginning of the second stage. Six women completed the second interview and five women were interviewed for the third time. With the use of grounded theory method, data was analyzed by constant comparative method.

Results: A substantive theory of the psychological adjustment of Chinese women to the impact of breast cancer was developed. Reframing was the core variable. A typology was constructed by using two contextual conditions (i.e., focus and approach). Four modes of coping were identified: fighting, following the natural course, struggling, and bearing.

Conclusion: These findings highlight the significance of understanding the women's interpretation of the situation. Adaptive coping depends on the coherence between the new frame and the women's existing frame system.

Multicenter Clinical Trials in Korea

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Purpose: The Korean Breast Cancer Society (KBCS) launched the clinical trial committee in 2001 and designed KBCS-01 protocol. After successful completion of KBCS-01, KBCS have launched 3 more multicenter clinical trials.

Methods: A phase II study of neoadjuvant docetaxel plus doxorubicin (KBCS-01) in stage II, III breast cancer. Ninety women were enrolled. Patients underwent 3 cycles of neoadjuvant chemotherapy with doxorubicin 50 mg/m² and docetaxel 75 mg/m² every 3 weeks, and followed by curative surgery. Primary end point of the study was clinical response, breast conservation rate and toxicity profiles. A phase IV, multi-center, open label, single arm clinical trial to evaluate the relationship of bone remodeling markers for skeletal complications in metastatic breast cancer patients (KBCS-02). The primary endpoint is to find the correlation between bone turnover markers and the frequency of skeletal-related-events for one year. A total of 237 patients will be included from 20 centers. Assessment of Quality of Life in postmenopausal patient with Letrozole (Femara®) as an early adjuvant treatment (KBCS-03). Approximately 587 patients from 32 centers will be enrolled in this study. Korean Hereditary Breast Cancer Study (KBCS-04) This center cohort study will be continued for more than 5 years through most university hospitals.

Conclusion: Multicenter clinical trials have not been active in Korea by the year 2000. Most clinical trials of breast cancer confined to single institutional design with small number of patients. From year 2001, number of institutions in Korea began to actively participate multinational multicenter phase III clinical trials.

Multicenter Clinical Trials in Japan

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There are several trends currently in the clinical trials of breast cancer in Japan. Firstly, many institutes and investigators have become to participate in the international global trials, which is remarkably different as compared with 10 years ago. It is evident that fundamentals for clinical trials such as involvement of clinical research coordinators have improved significantly. Secondly, investigator-driven clinical trials, particularly focusing on primary breast cancer, have been activated. For instance, several neoadjuvant studies have been conducted by nationwide groups such as Japan Breast Cancer Research Group (JBCRG). Several important findings have been generated by these activities. Thirdly, the correlative researches such as biomarker studies have become popular. Not only clinicians but also basic scientists have become enthusiastic about translational clinical researches. For the near future, it is obvious that we need to have local friendship and global partnership in further depth. In this session, these aspects will be touched upon.

On-going Clinical in NSABP

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NSABP clinical trials for breast cancer have gone through cycles of division and unification based on available targets and agents as well as evolving understanding of breast cancer biology.

While ER status no longer seemed to matter when B-20 demonstrated benefit from chemotherapy even in N-ER+ patients, and neoadjuvant trials were designed to unify trials, availability of aromatase inhibitors and prognostic factors such as OncotypeDx has made it impossible to conduct clinical trials including all patients.

Furthermore, approval of trastuzumab in adjuvant setting and continued interest in improving outcome of HER2 positive patients has resulted in division of trial population into HER2 positive versus HER2 negative, and ER positive versus ER negative, as well as high risk versus low risk node ER positive tumors. In this complex setting, clinical trial design is a complex process requiring close collaboration among clinical trial groups, NCI, and pharmaceutical industry. Trials such as TAILORx trial incorporating molecular testing add another layer into that complexity.

In this talk, on-going trials by NSABP and personal perspective on future directions of NSABP clinical trials will be discussed.

Current and Future Directions for Clinical Trials in Breast Cancer

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Major advances have been made in the treatment of breast cancer in the past three decades. The collaboration between basic scientists, patient advocates, and clinical providers has accelerated our acquisition of trial data and new therapeutic options. The most significant accomplishments in the field of clinical trials in the past few years revolve around early decision making trial design, neoadjuvant trials, and incorporation of predictive biomarkers.

Innovative clinical trial design includes randomized screening phase II designs as well as factorial trial designs. Examples of randomized phase II designs include trials in MBC of docetaxel alone versus docetaxel in combination with trastuzumab (Marty, JCO, 2005) or docetaxel alone versus docetaxel plus axitinib (Rugo, SABCS, 2006). Factorial designed trials include ECOG 1199 (Sparano, ASCO, 2007) or CALGB 9741 (Citron, JCO, 2003). Finally, trials focused on a specific population of breast cancer patients have played a role in current clinical trials. These types of trial designs will be discussed.

The neoadjuvant setting has also played a critical role in recent clinical trial design. Studies such as Gepartrio, NSABP B-27, and the ongoing neoadjuvant trials will be discussed and their unique designs and correlative science endpoints will be highlighted.

Incorporation of predictive biomarkers will play an essential role in the development of targeted agents in breast cancer. Successful examples of incorporation of predictive biomarkers include the study of lapatinib in IBC (Spector, JCO, in press) or bevacuzimab in MBC (Miller, Proc. Of American Society of Clinical Oncology, 2006). Tailor RX and its unique trial design serves as a model for future predictive marker trials. Finally, trials of real time pharmacodynamic and pharmacogenomic endpoints will begin to enroll in 2007 and the design of such trials will be discussed.

Internal Mammary Lymph Nodes Irradiation in Radiotherapy for Breast Cancer

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The inclusion of internal mammary nodes (IMN) in a radiotherapy (RT) field is still a controversial issue in either breast conservation or total mastectomy cases. No conclusive data support IMN RT, and the practice of treating IMN is culture-driven rather than evidence-based. More complicated and sophisticated techniques are needed for IMN RT. Very low rates of clinically apparent IMN recurrence even in the patients who do not receive post-operative radiotherapy (PMRT), and the possibility of lung and cardiac morbidity associated with IMN irradiation deferred the application of IMN irradiation. However, some retrospective studies and two randomized trials in which IMNs were included in PMRT field showed survival benefit. If modern radiotherapy techniques can reduce the RT-related complication risk and chemotherapy can eradicate systemic micro-metastasis, the addition of irradiation to nodal areas with a larger burden of microscopic disease may improve survival by preventing systemic reseeding. As breast cancer is the most common female cancer in most industrialized countries, and large number of patients are involved, the question of whether to irradiate the IMN is of major importance for healthcare. To elucidate this clinical problem, the European Organization for Research and Treatment for Cancer RT group performed a large multi-center trial, randomizing 4004 patients with postoperative breast cancer (stage I-III, node-positive and/or medial tumor) between RT to the IMN + medial supraclavicular fossa and no RT to this region. Patient accrual has been completed, but several more years are required to mature the results.

In our institution, the IMNs were included in PMRT field since the 1970s. During the 1980s-early 1990s, PMRT was not generally applied. In that period, most oncologists believed that chemotherapy could prevent loco-regional recurrence as well as distant metastasis. As a result, we experienced a lot of loco-regional recurrences including parasternal internal mammary lymph node recurrence. Since the late 1990s, PMRT was applied in the patients with breast cancer who had a tumor, more than 5 cm, or 4 or more axillary lymph node involvement. We analyzed the results of the patients with breast cancer who received systemic chemotherapy and PMRT with a consistent radiotherapy technique including IMN, and compared the results of patients who did not receive IMN irradiation.

Current issues involving IMN RT, radiotherapy techniques for IMN RT, and recent clinical data of IMN RT will be presented.

Multidisciplinary Care for Breast Cancer

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Purpose: The multidisciplinary team working is well known to be important in health-care delivery. The patients with breast cancer and their family require the biological-psychological-ethical-social-economical support. Here, we present our team approach to establish multidisciplinary care for the patients with breast cancer.

Methods: We have been constructing our multidisciplinary team for the patients with breast cancer since 2003. The voice of the patients was analyzed and several tools to improve patients-physicians relationship were made.

Results: Based on the Questionnaire as for worry and anxiety of 7,855 patients with malignant disease, including 1,904 breast cancers, psychological aspects such as anxiety occupied half of their problems. For the patient's satisfaction, supporting system is necessary, both for the physics and psychological aspects. Our multidisciplinary team has approached to care them, with the team pass and leaflets. These leaflets regarding to psychological support and sexuality are useful for care of the patients and improvement of communication between patients and medical staff. The five following points seem to be important: 1) Understand patient's needs, 2) Clarify responsibility, 3) Respect each other, 4) Maintain good communication, 5) Listen to the voice of patients and their family, and Update the system.

Conclusion: A team approach to multidisciplinary medical treatment and care contributes to achieve the patient's satisfaction. We consider that communication skill is important for good relationship between patients and medical staff. Guideline for psychosocial support is necessary.

Bisphosphonate Therapy for Breast Cancer with Bone Metastasis

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Introduction: Breast cancer is one of the most common cancers to develop bone metastasis. About 70% of deaths from breast cancer have bone metastasis. About 20% of these patients have metastasis limited to the bone without metastasis to other organs, and the disease progression is slow with an average life expectancy of 2 years and a five year survival rate of 40%. Metastasis is frequently seen in the spine, femur, pelvis, and humerus. Most breast cancer bone metastasis tend to be osteolytic and about 15% appear to be osteoblastic.

One of the most common symptoms of bone metastasis is bone pain further progressing to pathologic bone fractures. 30% of breast cancer patients with bone metastasis develop hypercalcemia due to bone destruction and complications from spinal cord compression may also appear.

The median time from diagnosis of bone metastasis to first skeletal complication was 27 months overall while the median time and the median survival time was 11 months, 26 months respectively in cases where only bone metastasis was involved. Osteolytic activity due to bone metastasis are caused by tumor-derived PTHrP. Bone metastasis induced osteolysis causes TGF- β release from the bone in which in turn increases PTHrP resulting in activation of osteoclasts and aggravating bone destruction. IL-1, IL-6, TCF- α , aside from PTHrP, also activates osteoclasts. Development of osteoclasts are induced by the RANK ligand which is a TNF cytokine derived from bone marrow stromal cells or osteoblasts. The precursor cells of osteoclasts have RANK ligand receptors therefore osteoclast differentiation and activation occurs on binding. On the contrary a TNF cytokine, OPG (osteoprotegrin) represses the RANK ligand. Therefore the characteristics of the bone metastasis depend on the action of these two factors.

Bisphosphonate: Bisphosphonate, a derivative of pyrophosphate, binds with osteoclasts to decrease bone destruction and in vitro inhibits the formation and secretion of lysozymes and represses the production and maturation of osteoclasts by altering the morphology. Bisphosphonates have also been reported to induce apoptosis of breast cancer cells and inhibit the invasion of cancer cells. The inhibitory activity of osteoclasts differs depending on the structure of the bisphosphonate. Drugs with amino groups are more effective than drugs without amino groups. Amino bisphosphonates have an inhibiting effect by blocking the mevalonate pathway causing repression of

protein prenylation and leading to structural and functional alterations of the osteoclasts resulting in osteoclast cell death. In vitro zoledronic acid was the most potent bisphosphonate with prenylation inhibitory activity. Bisphosphonates induces cell apoptosis through caspase activation other than blocking the mevalonate pathway and inhibits osteoclast activity by increasing OPG production from osteoblasts. Several biochemical tumor markers related to bone formation and destruction in bone metastasis may be beneficial in diagnosis and treatment. Bone specific ALP and PINP are bone formation markers and NTX, CTX, PYD are bone absorption markers detected in urine. These biochemical markers are useful in monitoring the effects of bisphosphonate therapy and NTX has been reported to be the most sensitive.

(1) Clodronate; Elomaa et al. have reported that clodronate reduced bone pain, formation of new osteolytic lesions, pathologic fractures and hypercalcemia. Iveson et al. reported that 133 patients who randomly administered oral clodronate 1,600 mg daily had significantly lower new bone metastatic lesions compared to the control group. Diel et al. reported that compared to the control group, 302 patients with micrometastasis given 1,500 mg oral clodronate daily for 2 years were found to have a lower incidence of distant metastasis, bone metastasis, visceral metastasis and had an increased survival rate. After 53 months of follow up of 288 patients, the clodronate group was found to have a lower bone metastatic rate and mortality rate but no improvement in visceral metastasis was found. Clodronate is effective in pain control in bone pain but IV clodronate was more effective than oral clodronate and the oral form has poor bio-availability.

(2) Pamidronate; There is an IV form and is effective in the reduction of bone pain, bone fractures and the frequency of radiation therapy and hypercalcemia. Pamidronate may delay first recurrence in bone and reduces complications. Pamidronate was effective in osteolytic bone metastasis and in patients with osteolytic bone metastasis patients on hormone therapy and pamidronate had less skeletal morbidities than the control group. Pamidronate prolonged the time to first skeletal complication in patients with bone metastasis on chemotherapy compared to the control group and reduced bone pain. 90 mg of pamidronate is intravenous infused for more than 2 hours, at 3-5 week intervals.

(3) Zoledronic acid; The osteoclast inhibitory effect of is very powerful compared to pamidronate. In the hypercalcemic mice models its control ability has been reported to be 850-1,000 times stronger compared to pamidronate. Hypocalcemia was achieved faster and longer compared to pamidronate in hypercalcemia. In bone metastatic patients 15 min - intravenous infusion of zoledronic acid (4 mg) every 4 week was effective as intravenous infusion of pamidronate (90 mg) every 4 weeks. Zoledronic acid has an advantage of having effect in any form of bone metastasis.

(4) Ibandronate; Ibandronate is a single amino biphosphonate which is commonly used in Europe, Body et al. reported that decreased SMPR was found in groups with intravenous infusion of Ibandronate (6 mg) every 60-96 weeks compared to the control group. Tripathy et al reported that oral ibandronate (50 mg) daily for 96 weeks showed a 20% decrease in SMPR. Both oral and intravenous forms of ibandronate are effective in reduction of all bone pain and skeletal complications and has an advantage of having little nephrotoxicity due to low tissue accumulation. Oral ibandronate is smaller in size and dose compared to clodronate that bioavailability and gastrointestinal side effects were greatly improved. Therefore oral ibandronate may be superior in improving the quality of life in bone metastasis patients. Recently studies comparing zoledronic acid to oral and intravenous ibandronate reported similar effectiveness as zoledronic acid.

Conclusion: Caution is required in bone metastasis because it may accompany complications such as fractures, neurological symptoms, and hypercalcemia. Chemotherapy or hormone therapy is needed in cases of bone metastasis and combination therapy of biphosphonates may delay the development of bone fractures and control pain while reducing other complications. In cases of only bone metastasis, disease progression may be prolonged therefore when extended clinical use is indicated, a well tolerated therapy with few complications is needed. Recently studies on adjuvant therapy and combined biphosphonate therapy in chemotherapy with bone loss are being carried out and in the near future a new biphosphonate treatment protocol for prevention and treatment of bone metastasis may soon be proposed.

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Brain Metastasis and HER-2 in Breast Cancer Patients

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Survival from metastatic breast cancer has improved over the past 2 decades. This improvement is related to an earlier time of diagnosis of MBC as well as more effective therapies. As survival from MBC improves, the problem of breast cancer-related brain metastasis will increase. Women with HER-2 + MBC have a higher incidence of brain metastasis, and there are multiple hypothesis for this higher incidence: 1) effective therapies that keep non-brain related disease from progressing, 2) a higher incidence of metastatic disease arising from HER-2 + early stage breast cancers, and 3) a tropism for HER-2 + disease to grow within the brain (Bendell, JCO, 2003).

Lapatinib (Tykerb) has recently been demonstrated to have activity in HER-2 + brain metastasis (Lin, Proc. American Society of Clinical Oncology, 2007) as well as lower the incidence of disease spread to the brain (Geyer, NEJM, 2007). Data for the completed studies with lapatinib as well as on-going studies will be presented. In addition, novel strategies for the treatment of HER-2 + brain metastasis will be presented.

Breast Cancer and Diet

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Cancer is a growing health problem around the world. Especially, breast cancer is the commonest form of cancer among women in the US, almost all of Europe and Korea. For breast cancer, nutritional effect may changes endogenous hormone levels, and may have direct impact on breast cancer risk [1].

Obesity is known as a well-established risk factor for breast cancer, colon cancer, renal cell cancer, adenocarcinoma of esophagus, and endometrial cancer. Obesity has a complicated relationship to both breast cancer risk and worse prognosis after disease onset. Obesity results in a worse prognosis in both overall and disease-free survival, in most studies of women with breast cancer [2-4]. Generally, it is known that the relationship of body mass index (BMI) with breast cancer risk differs by menopausal status [1]. However, the adverse prognostic effect of obesity on breast cancer is seen both in post-menopausal women and pre-menopausal women [5-7]. The association between obesity and hormone receptor status of breast cancer is quite complex. Some studies reported that increased mortality in obese women has been shown to be associated with both hormone receptor-positive and hormone receptor-negative breast cancer [8-10]. Mechanism of poor prognosis of breast cancer in obese women is possibly due to the delayed detection, impaired cellular immunity, less efficient chemotherapy and higher estrogen levels [11]. Although some studies showing no effect of obesity on breast cancer [12-14], obesity is considered as a preventable risk factor for death among breast cancer patients. Interventions that encourage weight control should improve the survival rates of patients with breast cancer.

Phytoestrogen is another important topic about food and breast cancer. Phytoestrogens are plant-derived chemicals that have estrogenic or antiestrogenic activity [15]. The most widely investigated phytoestrogens are quercetin, genistein, daidzein, flavanone etc. The most important question about phytoestrogen is whether phytoestrogens are promoters or protectors of breast cancer. If they are promoters, then we must assume that it is due to their estrogenic effect. If they are protectors, then other actions of phytoestrogens, including their ability to inhibit enzymes that are responsible for converting androgens and weak estrogens into estuarial, must be considered [16]. Results from epidemiologic studies, laboratory investigation and human experiments are very controversial [17-33]. Taken together results of all investigations, there is experimental

evidence for both a promotional and a protective effect of phytoestrogens on breast cancer. There is also no conclusive evidence that dietary intake of phytoestrogens in terms of the reduced incidence of breast cancer or the increased risk of breast cancer. Further study is required to determine the cellular actions of phytoestrogens beyond the estrogen receptor and the effects of combinations of different phytoestrogens during long-term exposure [34].

Vitamins are organic nutrients. Most research on vitamins and breast cancer to date has focused on vitamin A, carotenoids, vitamin E, and vitamin C [35]. Epidemiologic evidence on the role of vitamins in the risk of breast cancer is controversial. However, some studies supported that some vitamins might have a role in the prevention of breast cancer.

Phytochemicals are substantial anticarcinogenic and antimutagenic properties[36]. Curcumin (Turmeric), Capsaicin (Chilli peppers), Epigallocatechin-3-gallate (Green tea), Resveratrol (Grape), Caffeic acid phenethyl ester (Honey), Diallyl sulfide or triallyl sulfide (Garlic), Sulphoraphane (Broccoli) etc. are being investigated about both chemopreventive effects and chemotherapeutic effects.

Epidemiological studies have consistently shown that alcohol consumption is associated with a moderate increase in the risk for breast cancer [37]. Recurrence and mortality of breast cancer are also related with the consumption of alcohol [38].

Cancer survivors seek ways to minimize the risk of recurrence and death from breast cancer. However, people who depend upon unconventional treatments alone may lose valuable treatment time and reduce their chances of controlling their cancer and getting well. Despite complex and at times controversial data, proper diet program should be a part of the strategy to prevent the occurrence, recurrence and death from breast cancer. Food is a good complementary medicine, a complementary medicine is your good food. I am what I ate.

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Traditional Chinese Medicine for Breast Cancer Treatment

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Purpose: A comprehensive introduction of integrative medicine, especially traditional Chinese medicine (TCM) in the use of breast cancer treatment.

Methods: A review including TCM general introduction, Indications of TCM in cancer treatments, Advantages of TCM, TCM Theory and its Philosophy, TCM methods for breast cancer, etc.

Results: TCM Theory is important in breast cancer treatment, which includes six main theories, i.e. Yin Yang Theory; Individual treatment based on differentiation of symptoms theory; Zhang Fu inter-acting and counter-acting of Five Elements theory; Nature, Society & People in One System theory; Treatment based on TCM disease Progress theory, Preventive treatment of Progress Disease theory. TCM methods including TCM herbs, acupuncture, moxibustion, Qigong (breathing exercise) and Diets are of good effects in combining with breast cancer treatment, e.g. radiotherapy, chemotherapy, etc. and in alleviating the side-effects of radiation and/or chemotherapy and in improving patients' quality of life (QOL), etc.

Conclusion: The differentiation of western medicine (WM) and TCM are: TCM holistic-based; WM disease-based. Integration of chemotherapy, radiation and TCM Herbs or other treatment modalities together may benefit to patients, offering longer overall survival and better QOL.

Phytoestrogen and Breast Cancer

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Purpose: Phytoestrogens are plant-derived chemicals that act like hormone estrogen. Based on that higher and prolonged exposure to estrogen is linked with increased breast cancer, the association of phytoestrogen on breast cancer risk was attracted widespread attention and has been investigated extensively until now. So we need to understand the effects of phytoestrogens more systematically because KOREA is one of nations consuming large amount of dietary soybean, a most important phytoestrogen-rich source.

Methods: I reviewed and categorized multinational epidemiologic reports, in vitro and in vivo studies, and human trials published from 1996 through 2007 that studied the effects of phytoestrogens associated with breast cancer.

Results: In epidemiologic studies, some researchers reported that higher intake of dietary phytoestrogens was associated with reduction of breast cancer regardless of menopausal status. It was some meaningful that higher phytoestrogen intake during adolescence was associated with a reduced breast cancer risk. However other epidemiologists insisted non-significant and so far as adverse effects of phytoestrogens on breast cancer risk. In vitro and In vivo studies also showed bi-phasic results according to experimentally hormonal milieu and dosages or chemical structures of phytoestrogens. In human trials using breast tissues and mammographic imaging studies did not showed any consistent results to determine clinical effects of phytoestrogens.

Conclusion: The controversy continues on the role of phytoestrogens associated with breast cancer. To establish definitively the effects of phytoestrogens, we need well-designed In-vivo studies and a long-term epidemiologic study in which cancer recurrence or survival is end-points.

Complementary Medicine & Breast Cancer in Malaysia

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Modern medicine is based on technology and science and is evidence-based. However traditional medicine as practiced in Malaysia is based on medical practice from the past where there is very little technology and no evidence. Despite this, there is widespread use of traditional medicine for acute conditions like fractures, to chronic conditions like diabetes, hypertension and cancer, partly due to uncontrolled advertising in the media on traditional medicine with anecdotal claims of cure without actual scientific evidence. Although the government does ban advertisements of TCM products for 20 diseases, including cancer, yet such advertisements still appear in the public media. In Malaysia, up to 50-60% of new cases of breast cancer in a general hospital in Kuala Lumpur present with advanced disease. The two main reasons for late presentation was fear of surgery and belief in traditional medicine. 60% of women presenting with advanced disease had used traditional medicine. The commonest traditional medicine used is herbal medicine followed by spiritual therapy in the form of 'live' surgery or making superficial 'cuts' on the skin of the breast. Besides traditional medicine, there is also 'natural therapy' which advocates detoxification, diet therapy, and a range of supplements. Traditional medicine is also used to complement conventional medicine i.e. during chemotherapy and radiotherapy to reduce the side-effects of treatment. The Ministry of Health has a committee on TCM comprising representatives from various TCM bodies. A body similar to the medical council needs to be formed to control the practice of traditional medicine in Malaysia.

Proteomic Approach to Discover Biomarkers in Breast Cancer

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Breast cancer is the most common malignancy in Korean women. Developments in breast cancer molecular and cellular biology research have brought us closer to understanding the genetic basis of this disease. Unfortunately, this information has not yet been incorporated into the routine diagnosis and treatment of breast cancer in the clinic. It is the goal of comprehensive, genome-wide, and proteome-wide approaches to identify clinically useful biomarkers that will accurately identify diagnostic subtypes and predict prognosis and treatment responsiveness of breast cancer patients. To meet this goal, we have been adopting three kind of genomic approaches: 1) SNP chip, 2) gene expression microarray, and 3) array CGH. In addition, we are attempting to directly discover biomarkers using various kinds of high-end proteomic technologies with Korea Institute of Science and Technology (KIST). Based on our experiences of single gene SNP studies for defining high risk group of breast cancer development, we are doing a large scale SNP study using Illumina SNP chip with 384 SNP from 40 DNA repair genes. For gene expression microarray, we have been doing co-work with Stanford University since 2002. Recently, our array CGH analysis with BAC clones could detect various genomic alterations in ER-positive breast cancers, and Recurrence group samples showed a significantly different pattern of DNA copy number changes than did Non-recurrence group samples. Now we extended the sample size and adopted higher resolution BAC chip for outcome prediction study. We also attempt to apply this technique for response prediction of neoadjuvant chemotherapy. Presently, there is an intense interest in applying proteomics to breast cancer biomarker identification. Our proteomic approaches include comparative analysis of protein expression in normal and tumor tissues to identify aberrantly expressed proteins that may represent novel markers and analysis of secreted proteins in cell lines, primary cultures, and tumor interstitial fluid, and urine to identify breast cancer specific proteins that may be detectable in biologic fluids. We have already listed 57 proteins differentially expressed in tumor tissues compared with normal tissues by HSA/IgG depletion and narrow range DIGE method. Different type of proteomic methods such as membrane fractionation and ICAT was also applied to tissue samples and produced differentially expressed list of proteins. We are particularly interested in tumor specific antigens which can be detected in biologic fluids. Using the concept of interactions of tumor specific antigens secreted by cancer cells with auto-antibodies produced by immune response in cancer patients'

serum, we performed 2D-immunoblotting and observed antigens and auto-antibodies which are specific to tumor and could be detected differentially in patients' serum compared with healthy controls'. With this proteomic approach, tumor specific antigens from various sources such as cell lines, primary cultures, and tumor interstitial fluid, and urine have been explored. Of course interpretation of large amount of proteomic results from a wide variety of different biologic samples and methodologies may be a hard work for lack of the overlapping in the selection of candidates. It appears to be really true from our experiences that biomarker discovery with genomic and proteomic approaches is a long and uncertain path. To handle the challenges, we are trying to incorporate genomic data with proteomic results and planning to perform repeated small scale validation studies of candidates this year. In conclusion, we expect, with these diverse genomic and proteomic approaches, to finally find a goldmine of useful biomarkers overwhelming classical markers. We are opened to all inter-institutional or international proposals for collaboration.

Gene Expression Profiling Results in Improved Classification of Breast Cancer

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Purpose: Breast cancer is presently classified based on tumor diameter, histologic type and grade, lymph node status and estrogen receptor, progesterone receptor and HER2 status. A more refined classification should be possible based on genetic alterations and gene expression profiles.

Methods: We have previously defined a gene expression profile of 70 genes that is predictive for a short interval to distant metastases (<5 yrs) in lymph node negative (LN0) patients. We have subsequently validated the prognostic value of this 70 gene profile in a cohort of 295 stage I and II breast cancer patients younger than 53 years of age.

Results: To test whether gene expression profiling can be used in clinical practice, we have performed a study in 16 hospitals in the Netherlands. For 427 lymph node negative breast cancer patients, the 70 gene prognosis profile was assessed; 50% of the tumors were shown to have a good prognosis profile. To identify gene expression profiles associated with response to chemotherapy, we are conducting neoadjuvant chemotherapy studies. Gene expression profiles are generated from core needle biopsies obtained before treatment and correlated with the response of the primary tumor to the chemotherapy administered. To date, no gene expression profile predicting the response of primary breast carcinomas has been identified, but we are currently expanding the series of patients in this neoadjuvant chemotherapy study.

Conclusion: We conclude that gene expression profiling is a method that will lead to improved classification of breast cancer by incorporating novel diagnostic tests that can be reliably implicated in clinical practice.

Genetic Polymorphisms of Estrogen Metabolizing Genes as Susceptibility and/or Prognostic Factors for Breast Cancer in Taiwan

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Several germline mutations in genes, such as p53, APC and BRCA1/2, have been identified in some rare familial cancer syndromes and common sporadic cancers. The cancer risk caused by each of these germline mutations can be very high, although the mutation or at-risk allele is rarely seen in the general population. In contrast, some germline mutations existing in genes that are involved in the pathways responsible for the metabolism of carcinogens, including nutrients, xenobiotics, and even estrogen, only increase the cancer risk several fold, but a mutation allele can be very common. Identifying genes involved in the metabolism of estrogen greatly increase the potential for understanding the molecular pathogenesis of breast cancer and, eventually, for its treatment and prevention.

The genes involved in the estrogen metabolism pathway, including CYP17 (estrogen biosynthesis), CYP1A1 (estradiol hydroxylation), and COMT (catechol estrogen inactivation) have been studied in order to understand whether estrogen could induce breast carcinogenesis via an initiating mechanism involving genetic damage caused by catechol estrogen. The breast cancer risk associated with individual susceptibility genotypes varied for the three genes, being highest for COMT, followed by CYP1A1, and, lastly, by CYP17. A trend to an increasing risk of developing breast cancer was found in women harboring higher numbers of high-risk genotypes ($p=0.006$), including the high-activity CYP17 (CYP17 A2/A2), high inducibility CYP1A1 (CYP1A1 MspI vt/vt), and low activity COMT (COMT L/L) genotypes. The results support the possibility that breast cancer in Taiwan can be initiated by estrogen exposure.

Hormonal therapy for breast cancer is aimed at lowering estrogen levels or blocking of estrogen receptors. Adjuvant tamoxifen for 5 years has been a standard for early breast cancer with positive hormone receptors. Genetic variants of CYP2D6 and sulfotransferase 1A1, both of which catalyze the formation of important metabolites of tamoxifen, have been shown to be associated with different survivals among patients treated with adjuvant tamoxifen. Aromatase inhibitor has also shown its efficacy in reducing the risk of recurrence and/or death in postmenopausal patients with hormone-responsive early breast cancers. In premenopausal women, estrogen is mainly produced by the ovary, and aromatase catalyzes the final step of the conversion of androgens to

estrogens. In postmenopausal women, the ovary ceases to function and aromatization of androgen in extragonadal tissue becomes the main source of estrogen. Aromatase is encoded by the gene CYP19. A (TTTA)_n tetranucleotide repeat polymorphism within intron 4 of CYP19, has been examined for an association with breast cancer risk and the prognosis of early breast cancer. An increasing repeat number was found to be associated with longer breast cancer survival in a British population-based study. Our study also revealed that CYP19 (TTTA) repeat polymorphism is associated with the survival of premenopausal HR-positive breast cancers. The findings can be explained by the association between variant alleles of CYP19 and estrogen levels. These studies suggest that pharmacogenetic assessment may be able to evaluate who will benefit from hormonal therapy.

Tumor-stromal Interactions in Breast Cancer Metastasis

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Purpose: Despite significant advances in the clinical management of breast cancer, metastasis is the major cause of death of women with this disease. Two basic principles have become apparent from studies of the pathophysiology of metastasis. First, tumors are heterogeneous; thus, different cells from the same tumor can differ in their potential to metastasize. Second, the metastatic process is a well-orchestrated sequence of events that depends on the properties of the tumor cells and their interactions with the micro-environment at the metastatic site.

Methods: We have developed xenograft models using immunodeficient mice to investigate breast cancer metastasis in different organs sites, including lung, brain, and bone. To test the general hypothesis that breast cancer cells that survive and grow in a metastatic site are unique populations of cells, we established a variant of the MDA-MB-231 cell line from three cycles of injection into the carotid artery and selection of the resulting brain metastases.

Results: A panel of genes was identified as differentially expressed in the brain-metastasis derived cells, including increased expression of VEGF/VPF. Reducing VEGF expression in the breast cancer cells abrogated their ability to extravasate through endothelial cell monolayers in vitro. Treatment of mice injected with the brain-metastasizing cells with an inhibitor of the VEGF-receptor tyrosine kinase resulted in reduced brain tumor burden and reduced microvessel density within the tumor lesions.

Conclusion: Our study illustrates how targeting interactions between cancer and stromal cells, in this example mediated by the angiogenic cytokine VEGF, can restrict the metastatic progression of breast cancer cells.



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Survival Session

Positive Outlook; Living with Cancer – Preparing for Life after Breast Cancer Treatment – The Value of Survivor Retreats

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Purpose: A great deal of time and caring is spent while the patient is going through active breast cancer treatment. When her treatment is completed she may feel insecure, fearing recurrence, unable to emotionally move forward to live a healthy and productive life. This has been a life altering experience. Most women feel some degree of depression and uncertainty as they complete their treatment. The purpose of the survivor retreats are to help them re-engage in their lives emotionally and physically healthier, seeing themselves now as a survivor and not still as a fragile patient.

Methods: As part Hopkins Breast Center's patient satisfaction surveys, we ask women post treatment 82 questions to measure their experience with us. Several questions related to psychological well being after treatment. 1) how well informed were you about the psychological and social problems breast cancer and its treatment? Hopkins 58.5%; elsewhere 38.5%; how effectively were the psychological needs addressed post treatment? Hopkins 58.3%; elsewhere 37%; how well prepared were you for any of the concerns you had after treatment was completed? Hopkins 68.5%; elsewhere 46.5%

Results: Program is a two day overnight stay retreat focusing on stress management, moving forward, yoga, humor, talk therapy, wellness, and transforming her from a patient into a long term survivor. A tree of life and hope is created. Women are surveyed 6 months later.

Conclusion: How well do you feel you are psychologically adjusting post treatment: before retreat- 42%; after retreat- 70%. We now hold these annually, entering our 8th successful year.

Advocacy & Communication

Ranjit Kaur¹

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Advocacy starts from oneself in which the individual has a felt need and experiences the difficulty or the gaps that exist as opposed to perceived needs which are recognized by observation or communication with a third party. Advocacy in breast cancer has originated from the personal battles of individuals with breast cancer, who have felt the need for improving the quality of lives for others experiencing the same ordeal. It can help influence policies, standardize and make available equity in healthcare systems, create a socio-cultural change regarding attitudes, facilitate communication and break down barriers. This paper examines the different levels of advocacy in breast cancer that exists globally. Basic advocacy is seen at community grassroots level where each individual is supported in through diagnostic, treatment and recovery process. National and international movements are also formed to influence policies and negotiate with the authorities particularly to reinstate the basic human rights of the individual living with breast cancer. Examples of the different levels and methods of advocacy and the unique role as activist of individuals with breast cancer will be described in this presentation.

Sharing Breast Cancer Experience

Wae Ryun Kim¹

¹*Korea Breast Cancer Patients Society, Korea*

Purpose: This lecture is to give hope, inspiration and courage to those who are suffering from breast cancer by sharing precious experiences I had from a long recuperative practice.

Methods: The method is basically qualitative, giving oral statement on the past experiences. The statement is about how to study and practice the status of maintaining a stable triangle supported by your body, mind and the spirit which is believed to strengthen the immune system. Specific examples of this practice are change of eating habits, exercise, management of stress, mind control and some creative activities which can render you delight together with a sense of fruitfulness in labor.

Results: One might be surprised to know that how fast I recovered from my sickness although treated with high dosage. Moreover, I have become much healthier than I had been before I fell sick. Therefore, it comes up naturally to my mind that the breast cancer was rather a blessing to me because it helped me find a true happiness through the illness.

Conclusion: You can overcome your sickness through practicing mind control. Life-span of a human being may not be changed by herself or himself: and yet, the quality of life depends on how you practice with your own mind. You will reach to the happiness through listening and following the voice of your mind. You will be able to feel a deep 'mindfulness' when you find your own way of life from the bottom of your heart.

Survivor's Activities in Japan

Takako Watt¹

¹*Japan Breast Cancer Network, Japan*

The Japan Breast Cancer Network is a patient support group with members all over Japan. Our motto is to live life again with dignity and hope after breast cancer operation. To show that you can live life as beautifully as you did before is very important. It will change people's misconception that one cannot have the same kind of life as before you had cancer. Our group is also very active in the public education area. We believe that we, who have had breast cancer, can lessen the number of breast cancer deaths because experience is the most powerful tool to persuade people. By showing that we have survived, we can lessen the fear of women to do self examination or go to see the doctor. In my presentation, I would like to introduce and describe what we do for this purpose.

Overcoming the Fear of Recurrence

Laura Tsai¹

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Purpose: All breast cancer survivors are fearful of recurrence and the associated threatening of death. The fear emerges shortly after diagnosis, and it usually increases in extent with time and may last endlessly. How to lessen the fear through outside helps is extremely meaningful for the survivors to regain a brighter life.

Methods: Surveys aimed to understand the survivors' fears and needs were made by this Association. We also participated in a national survey sponsored by the Taiwan Breast Cancer Alliance in 2005 to study survivors' responses to support groups.

Results: Our investigation indicated that causes of survivors' fear of recurrence, aside from the threatening of death, include the painful medication process, lack of understanding the disease and their own health condition, and lack of source of help. TBCA's survey showed more survivors obtain help from support groups (55.6%) than from medical specialists (41.3%). After joining the support groups, 80-90% of the survivors are more self-affirmative and confident in recovery. They also enjoy better human relationship and life quality. Consequently, the fear of recurrence is significantly lessened. Our study further revealed that encouraging survivors to become volunteers is a positive way to relieve psychological pressure. Volunteers have the sense of accomplishment by helping other patients and the feeling of satisfaction by having their own stages to perform.

Conclusion: This presentation explains how the support groups help survivors and how the survivors respond to support activities. The combined effects on reducing fears of recurrence are discussed, and the comments of several survivors/volunteers are introduced.



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Poster

Knowledge and Quality of Performance of Breast Self Examination in Two Group of Employees in Shiraz University

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Purpose: To study knowledge and quality of performance of breast self-examination in two groups of employees in shiraz university of medical sciences.

Methods: One hundred and forty health workers and 161 nurses who met the research criteria participated in this survey. The data collection was done in two stages. First, data were collected by questionnaire. The first part contained demographic questions, the second and third parts contained questions on knowledge of breast cancer and BSE. In the second stage, quality of performance of BSE was evaluated by a check list.

Results: The data analysis showed that two groups had moderate knowledge about breast cancer and BSE. There was no significant difference in knowledge of breast cancer ($p=0.11$) and breast self-examination ($p=0.39$) between two groups. Quality of performance of breast self-examination was unacceptable according to grades, and t-test revealed no statistically significant difference between two groups ($p=0.25$). Knowledge of BSE was significantly associated with age, level of education and working experience. Quality of performance of BSE was significantly positive in association with knowledge of breast cancer and BSE, frequency of breast self-examination performance and confidence in performing it correctly.

Study about Mammography Test Performance in Rasht's Women

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Purpose: Breast cancer is the most prevalence women cancer in the developmental countries and increase in under developmental countries, too. The aim of this study on mammography test performance in the rasht city's women

Methods: It is descriptive cross-sectional study and from rasht city 1,200 women, 40 years age and older selected by a clustered random sampling, and from each cluster women were chosen randomly and equally for research. The collection of data and information was done using questionnaires and interview. Then, the findings and results were analyzed with a chi-square test.

Results: The findings and results of this survey showed that 42/50% had performed the mammography test, and 18/24% regularly done this test. The most important reason of the women to performance mammography test was observation disease and some symptoms in themselves. The results of this survey also showed that the most important reason for non performance or irregular performance mammography test by the women was not pain and disease in themselves. The majority of women in this study (77/50%) suggested that, the education about the breast cancer and mammography test is necessary for women. They believed best kind of give this information by radio and TV.

Conclusion: It is necessary that the health personnel give correct and suitable information and education to women about importance opportune and regular performance mammography test for preventive breast cancer that result is decrease of mortality rate from this disease.

Differences in Knowledge, Risk Perception and Early Detection Behavior of Breast Cancer between Normal and Borderline Risk Groups

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Purpose: The purpose of this study was to identify the distribution of according to the score calculated with the Breast Cancer Risk Appraisal, to investigate differences in knowledge and risk perception on breast cancer, and to investigate differences of the stage distribution of early detection behaviors and abnormal breast conditions by mammography between groups.

Methods: Using convenience sampling, 424 rural women were selected. To measure knowledge and risk perception, a dichotomy scale of 8 items and a 4 point Likert scale of 6 items were used, respectively. Stage of early detection behavior (BSE and mammography) was measured by a single question asking each woman where she was in the five stages for BSE and six stages for mammography.

Results: According to the Breast Cancer Risk Appraisal, 60.1% of the participants was fell into the normal group, and 39.9% was borderline risk group. Scores of knowledge and risk perception on breast cancer in the borderline risk group were significantly higher than those of the normal group. There were no significant differences in stages of early detection behaviors between two groups. There were no significant differences in distribution of abnormal breast conditions between two groups.

Conclusion: The findings showed that knowledge and risk perception were higher in the borderline risk group than the normal group, while there was no significant difference in early detection behavior between two groups. Therefore, in order to enhance and reinforce the early detection behavior, interventions should address strategies monitoring and facilitating one's behavioral stage of change as well as cognition.

A Clinicopathological Study of Intraductal Papilloma: Is it Premalignant Lesion? or not?

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Purpose: Intraductal papilloma is the most frequent pathological findings in women with pathologic nipple discharge. These are often considered to be a premalignant lesion. This study analyzed the clinicopathological characteristics of intraductal papilloma.

Methods: A retrospective review was performed of 44 patients who underwent an operation for intraductal papilloma between 1992 and 2007.

Results: The mean age was 44 years old (19-67 years), the mean follow-up period was 108 months (17-205 months). Of the 44 patients, 34 (68%) had nipple discharge. Twenty-four (70.6%) had bloody discharge, 8 (23.5%) a serous discharge, and two had yellowish discharge. The majority of patients presented with an ipsilateral palpable mass. The positive predictive value of breast ultrasonography, fine needle biopsy, and US-guided core needle biopsy was 74%, 31%, and 100%, respectively. The four lesions were removed by microdochestomies, 39 by local excisions, and one through breast conserving surgery. The majority of papilloma was the solitary type (75%) and central type (82%). Four carcinomas were developed in the follow-up period, and all presented palpable mass. Although there was no significant statistical difference, cancer was more developed in multiple and peripheral types. Three of them were papillary carcinoma on same quadrant of previous excision site, and one was an invasive ductal carcinoma on a different quadrant of a previous excision site. There were no lymph node metastases in all four cancer patients.

Conclusion: Microdochestomy has been the accepted standard treatment for intraductal papilloma. But local excision and long-term close follow-up should be considered for multiple and peripheral type intraductal papilloma.

Effects of an Integrated Breast Health Program according to Stages of Breast Cancer Risk Appraisal

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Purpose: The current study evaluated the effects of an integrated breast health program according to the levels of breast cancer risk appraisal on knowledge of breast cancer, early detection behaviors, and diet patterns in Korean healthy women.

Methods: A non-equivalent control group pretest-posttest design was used. A total of 413 women aged 40-59, registered at the Life Long Health Center in two cities, were classified into normal groups of 249 women (intervention: 138, control: 111) and borderline-risk group of 164 women (intervention: 68, control: 96) according to their risk appraisal by Lee's model. The integrated breast health program was developed as basic and alarm type for normal and borderline-risk group. The program included education, counseling on breast cancer, early detection behaviors, and appropriate diet with multimedia and individual practice session using breast models according to levels of risk appraisal. The knowledge on breast cancer, early detection behaviors, and diet pattern were used using questionnaires at baseline and three months after the intervention.

Results: In both normal and borderline-risk group, intervention groups reported significantly higher scores of knowledge on breast cancer ($t = -4.13, p = 0.000, t = -5.83, p = 0.000$) and higher stages of BSE behaviors ($t = 4.62, p = 0.000; t = 3.30, p = 0.001$) than control groups. Stage of mammography participation was significantly higher only in the intervention group of borderline-risk group.

Conclusion: The results showed positive effects on knowledge and early detection behaviors of breast cancer, except diet pattern in normal and borderline-risk groups. Further studies should investigate longitudinal effects of the intervention program on dietary change.

Methodology and Results of 5 Years Breast Cancer Screening in Situation of Limited Resources

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Purpose: Breast cancer is the most common malignancy among women in Estonia. Nationwide 5-year breast cancer screening program started in 2002.

Methods: The target group was women aged 50-59 with valid health insurance. In 2002 women were encouraged to participate through mass media. In 2003 personal invitations were introduced, self-referrals continued to be accepted. In 2004 screening became strictly invitation-only. The invitations are sent every year to certain birth year cohorts. For each year Health Insurance Fund allocated certain amount of money that enabled to screen corresponding amount of target population. Planning was complicated, because it depended on participation rate- the lower the participation, the more invitations had to be sent out to guarantee planned number of tests. Two-year interval was not achievable till 2005. In 2006 four year cohorts were invited for the second screening round.

Results: During 5 years 94,139 women were screened. In 2002 on self-referral basis, in 2003 58% participated with invitations, 42% on self-referral basis. Started 2004 all women participated invitation based only. The recall rate decreased from 5.9% (2002) to 2.18% (2006). 454 breast cancers were diagnosed, 343 (75.5%) of them in early stages (0-IIa). The average participation remained low, but increased from 37% (2003) to 51% (2006).

Conclusion: Due to the limited resources, methodology for organized screening program was implemented step by step. Cancer detection rate is good. Detection of early breast cancer is increasing; recall rate for assessment is decreasing. There are two main problems: low participation rate and lack of centralized database.

Teachers

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Purpose: To gather detailed information about the breast health status of the study population.

Methods: The questionnaire (self assessment form), comprised two sections based on ACS forms for assessing risk of breast cancer. Test analysis direction was placed at the end of Questionnaire as follows: Under 100 / low risk group 100-109 / moderate risk group 200 and higher / high risk group. The questionnaire was conducted to 4,830 teachers who were involved in teaching in high and guidance schools in Shiraz. 3,121 respondents completed and returned the questionnaires (a response rate of 65%). The non responders comprised women within the youngest age group.

Results: Among 3,121 participants 2,240 (71.7%) were in low risk group and 837 (28.2%) and 3 (0.09%) were in moderate and high risk group. Among the 2,367 women age 35 and older only 871 (36.8%) reported having setup mammogram baseline and follow up. 1,496 (63.2%) of women reported they were not in compliance with mammography screening guideline, 958 (64%) of them were in low risk group and 538 (35%) were in moderate risk for developing breast cancer that 232 (43.1%) of them referred to physician for mamography. Chi-square test with $p=0.00001$ confirmed the relationship between individual awareness about the degree of susceptibility for breast cancer and motivating women to refer for screening test. only 0.09% performed BSE on regular basis monthly.

Conclusion: The results acknowledge the importance of understanding own risk factors associated with referral for mammography.

The Effects of a Theory-based Intervention Emphasizing Breast Self Examination for Korean Women in the Community

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Purpose: Breast cancer has become the leading cancer among Korean women. Although breast self examination (BSE) is an important component of cancer detection, there is a lack of research on the effects of BSE educational programs among Korean women. This study aimed to identify the effects of a theory-based intervention focused on BSE (TBI-BSE), building on Bandura's self-efficacy theory, on breast cancer-related knowledge, health beliefs, and self-efficacy among Korean women in the community.

Methods: This study employed a nonequivalent control group pretest-posttest design (25 experimental, 34 control). Women between the ages of 30 to 60 were recruited from the community to participate in the TBI-BSE (three sessions, 2 hours each). Intervention content is described in table 1. The control group received educational materials only following completion of data collection. Pre and post-test data were collected on breast cancer-related knowledge, health beliefs, and BSE self-efficacy. Posttest data were collected 4 weeks following the first TBI-BSE session.

Results: The experimental and control groups were homogeneous in general and BSE-related characteristics at baseline, although the experimental group had slightly higher health belief scores ($t=2.71$, $p<0.05$). At post-test the experimental group demonstrated greater knowledge levels ($t=4.56$, $p<0.001$), BSE self-efficacy ($t=6.58$, $p<0.001$), and health beliefs as well, after controlling for health belief scores as ANCOVA ($t=4.19$, $p<0.05$) (table 2).

Conclusion: This study suggests that a BSE-focused intervention building on self-efficacy theory may be an effective outreach program for increasing breast cancer-related knowledge, health beliefs, and BSE self-efficacy for Korean women in the community. Recommendations for future studies are made.

Table 1. Description of the Theory-based Intervention emphasizing BSE (TBI-BSE)

Session	Method	Principle	Content	Resources
1	Discussion	Emotional arousal & Verbal persuasion	Emotional reaction to breast cancer and BSE	Pamphlet
	Lecture		Facts on breast cancer & BSE basics	Presentation
	Demonstration & Practice	Performance accomplishment		BSE Video & practice with breast model
2	Discussion		Experience of BSE or breast self-management	Pamphlet
	Lecture	Verbal persuasion	Breast cancer prevention (exercise, diet, stress, etc.)	Presentation
	Demonstration & Practice	Vicarious experience & Performance accomplishment	Breast lump beads activity: making cell phone accessory Review of BSE	Beads (various sizes) Breast model
3	Discussion		Experience of BSE or breast self-management	Pamphlet
	Testimony	Vicarious experience	Breast cancer survivor's experience	Testimony by survivor
	Practice	Performance accomplishment	BSE test, review of BSE	Breast model & whole body mirror
	Discussion & wrap-up		Evaluation of program, Q&A Conferring certificate	Certificate

Fig 1. TBI-BSE content

Table 2. Comparison of knowledge, health belief and self-efficacy after theory-based intervention

	Before (N= 25)	t	p	After (N= 34)	t or F*	P
	M=SD			M=SD		
Knowledge						
Experimental	11.08±2.34	1.15	.26†	13.72±1.40	4.56	.00‡
Control	10.44±1.93			11.50±2.33		
Health Belief						
Experimental	57.92±5.54	2.71	.01†	60.24±4.98	4.19	.045†
Control	53.53±6.56			52.85±7.72		
Self-Efficacy						
Experimental	30.16±8.56	-.45	.66†	42.72±6.16	6.58	.00‡
Control	31.12±7.75			31.82±7.21		

*Measured by ANCOVA in which the values of pre-tests were treated as covariance

†p < .05

‡p < .01

Fig 2. TBI-BSE effects

Analysis of Factors Related to Regular Mammography Screening in Jeju

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Purpose: This study was to identify factors affecting regular mammography screening behavior of outpatients.

Methods: The target subjects were 150 women who came to the breast clinic at the university hospital in Jeju, and the study period was around 10 months from March to December, 2006. The data were analyzed using descriptive statistics, Chi-square test, t-test, and logistic regression analysis.

Results: The experience of mammography was conducted in 50% of subjects and the rate of regular mammography performance was 31.6%. In the relational analysis between various factors and regular mammography, there were significant differences among the age 41-50 group; having a job; the high income group; the regular exercise group; the non-drinking group; previous x-rayed group, and the group with breast disease. And in the logistic regression analysis, those who prefer bean food are 3.20 times more likely to take mammogram regularly; those who are married are 3.49 times more likely to do than the unmarried. Also, the groups that have low health belief and are under age 51 were less likely to take regular mammogram.

Conclusion: Jeju seems to be excluded from the nationwide survey, so the study that analyzes the early check up for breast cancer of Jeju area in detail has a significant meaning. In order to increase the rate of conducting regular mammography, there must be different intervention strategies according to food habits, marital status, age group and support system must be devised to increase health belief about breast cancer examination behavior.

Prophylactic Mastectomy and Oophorectomy in a Brca1-Positive Patient

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Purpose: We report a case of prophylactic mastectomy (PM) and bilateral salpingo-oophorectomy (BSO) in a carrier of BRCA mutation.

Methods: The patient was a 39-year-old woman who was seen in a genetic counseling clinic for discussion of risk-reducing strategies of the breast and ovarian cancer. She presented at the age of 38 years with a 1.5 cm sized, grade 3, and ER/PR/HER2 negative infiltrating ductal carcinoma of the right breast. She was treated with a wide local excision of the right breast and sentinel lymph node biopsy of the axilla. She was then treated with CAF chemotherapy and radiation therapy. She was initially counseled at the time of surgery due to a family history of a mother with breast cancer at the age of 58. At the end of radiation therapy, we received a genetic test result and it was positive for the BRCA1 mutation (3746_3747insA). After the long discussion of cancer surveillance and risk-reducing options, she decide to proceed PM and BSO.

Results: Before surgery, psychiatric consultation was done and questionnaires evaluating depression, anxiety, body image, quality of life, and psychological distress were taken. After the long discussion with plastic surgeon, she decided to undergo delayed reconstruction of the breast. We performed endoscopic bilateral skin-sparing mastectomy and a laparoscopic bilateral salpingo-oophorectomy. There was no complication after surgery and the pathologic examination revealed no evidence of cancer in both breasts and ovaries.

Conclusion: This report acts as PM and BSO being the feasible risk-reducing options for the breast cancer patients with BRCA mutation in Korea.

Cancer Risk Estimates for Korean BRCA1 and BRCA2 Mutation Carriers

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Purpose: To estimate the risk of breast and ovarian cancer in Korean BRCA1 and BRCA2 carriers.

Methods: Using Kaplan-Meier analyses, cumulative cancer risk estimates were determined by analyzing 61 BRCA1 mutation carriers in 44 families and 47 BRCA2 mutation carriers in 32 families identified in 5 academic breast clinics.

Results: By age 70, female breast cancer risk in BRCA1 and BRCA2 mutation carriers was 90.7% (95% confidence interval [CI] = 82.3% to 99.0%) and 80.4% (95% CI = 67.2% to 93.7%), respectively, and ovarian cancer risk was 24.6% (95% CI = 0% to 50.3%) and 11.1% (95% CI = 0% to 31.6%), respectively. By age 70, bilateral breast cancer risk was 17.8% (95% CI = 4.48% to 31.1%) in 52 breast cancer patients with BRCA1 mutation and 16.6% (95% CI = 3.2% to 30.0%) in 35 breast cancer patients with BRCA2 mutation.

Conclusion: The penetrance of BRCA mutations in Korea is largely consistent with previous studies on Western populations. However, small number of the cases, high proportions of probands in the study subjects, short term follow-up, and large CIs are the limitations of the current study. Korean Hereditary Breast Cancer Study (KOHBRAS Study) may definitely answer this question.

Basal-like Cytokeratin Expression Profiles of Korean Hereditary Breast Cancers Having BRCA Gene Mutation

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Purpose: BRCA mutation tumor shows a distinctive morphology and immunohistochemical phenotype. This study evaluated the immunohistochemical profiles for characterizing triple-negative feature and a basal-like phenotype in Korean hereditary breast cancer having BRCA mutation.

Methods: Paraffin-embedded tumor samples from 213 breast cancer patients (165 no mutations and 48 mutations) who had taken BRCA mutation test were evaluated immunohistochemically using antibodies to ER, PR, HER2, EGFR, CK5/6 and CK14 (basal-like cytokeratins), and CK8 (simple epithelial-type keratin).

Results: Breast cancers having BRCA mutation were more often ER-negative ($p < 0.001$), PR-negative ($p = 0.03$), and triple-negative (ER/PR/c-erbB2) ($p = 0.004$) compared with no-BRCA mutation tumors. Basal-like cytokeratin, CK14 was significantly highly expressed in the BRCA mutation tumors (41.7% vs. 16.4%, $p = 0.001$) compared with controls. Expression of CK 5/6, however, did not show a significant difference (18.8% vs. 11.5%, $p = 0.225$). In contrary, expression of CK8 was prominent in the no-BRCA mutation tumors (93.3% vs. 99.2%, $p = 0.01$). In the group of triple-negative tumors, CK 5/6 ($p < 0.001$), CK 14 ($p < 0.001$), and EGFR ($p = 0.02$) were significantly highly expressed compared with the counter part. Characteristically, expression of CK 14 showed significantly differences between the groups of BRCA mutation or not ($p = 0.01$) as well as the groups of BRCA 1 and 2 mutations ($p = 0.04$).

Conclusion: Korean hereditary breast cancer having BRCA mutation has more often ER-negative, PR-negative, and triple-negative expressions. High expression of CK 14 indicates basal-like phenotype of the BRCA mutation tumors. CK 14 expression, not CK 5/6, is found as basal-like feature of Korean hereditary breast cancer.

Analysis of BRCA1 and BRCA2 Germline Mutations in High-Risk Korean Breast Cancer Patients

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Purpose: BRCA1 and BRCA2 are two principle hereditary breast cancer susceptibility genes. However, the prevalence of BRCA gene mutations among Korean women is not well elucidated. The purpose of this study was to evaluate the prevalence of BRCA1 and BRCA2 mutations among Korean high-risk breast cancer patients.

Methods: The study subjects consisted of 209 breast cancer patients from two genetic counseling clinics between Oct. 2001 and Jan. 2007. The indications of BRCA testing were breast cancer patients with family history of breast and/or ovarian cancer, early-onset breast cancer, bilateral breast cancer, and personal or family history of male breast cancer. The fluorescence-based conformation-sensitive gel electrophoresis and direct sequencing were used to detect BRCA gene mutations.

Results: Disease-causing mutations of BRCA genes were present in 13.4% (28/209) of the high-risk patients and the prevalence of BRCA1 and BRCA2 mutations are 3.8% (8/209) and 10.0% (21/209), respectively. The mutations of BRCA genes were most prevalent in patients having family history of breast cancer (25/134, 18.7%), followed by patients with personal or familial history of ovarian cancer (2/11, 18.2%), bilateral breast cancer patients (4/24, 16.7%), personal or familial history of male breast cancer (1/6, 16.7%), and early-onset breast cancer patients (8/82, 9.8%).

Conclusion: The prevalence of BRCA gene mutations in high-risk breast cancer patients was similar to the previous studies. However, the distribution of BRCA1 and BRCA2 gene mutation is reversed in this study and this needs further investigation.

The Acceptance Rate of BRCA1/2 Testing in High-Risk Breast Cancer Patients: Before and After the Medical Insurance Coverage

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Purpose: BRCA1/2 testing is the essential part of the management of hereditary breast cancer patients. In Korea, national medical insurance started to cover the costs of BRCA1/2 testing for the breast cancer patients at high risk of BRCA1 and BRCA2 carriage since Aug 1st, 2005. The purpose of this study was to evaluate the influence of the medical insurance coverage on the acceptance rate of BRCA1/2 testing in genetic counseling unit.

Methods: From July, 2003 to July, 2007, we performed 151 genetic counseling sessions for high-risk breast/ovarian cancer patients. We prospectively collected the database including the initial acceptance of the BRCA testing, cause of test-refusal, interval between surgery and counseling, and the institution where treated. Acceptance rate (AR) of BRCA test before and after insurance coverage was compared.

Results: Total AR was 91% (137/151) and the ARs before and after the insurance coverage were 74.5% (38/51) and 99% (99/100), respectively ($p < 0.001$). Before the insurance coverage, the AR is higher for the patients who received genetic counseling within 3 months of the surgery (44.4% vs. 15.2%, $p = 0.022$) and who were treated in our institution (44.4% vs. 15.2%, $p = 0.022$). Thirteen patients who were counseled before the insurance coverage refused testing due to high cost (10/13), preferred to choose frequent breast cancer screening (6/13), and deferred to answer (5/13).

Conclusion: The AR of BRCA testing increased markedly after the start of medical insurance coverage. Doctor should offer BRCA testing to the breast cancer patients at high risk of BRCA1 and BRCA2 carriage within 3 months of surgery.

LOH of Major Tumor Suppressor Genes in Invasive Ductal Carcinomas

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Purpose: The major tumor suppressor genes (TSGs) such as p16, Rb, E-cadherin and p53 may play important roles in cell cycle regulation, apoptosis and the regulation of the expression of other genes as well as tumor suppression. Microsatellite alteration such as LOH has been reported as a novel mechanism of carcinogenesis and as a useful prognostic factor in many malignant tumors. Also, LOH is known to be related with allelic loss of various TSGs. This study evaluated LOH of 4 TSGs in invasive ductal carcinomas (IDCs) and correlated these results with the clinicopathological factors.

Methods: LOH analysis was carried out using a polymerase chain reaction with 12 polymorphic microsatellite markers of 4 TSGs in 50 surgically resected tumors and their non-tumorous counterparts.

Results: LOH was detected in 86% of 50 cases of IDCs. LOH results detected on all chromosomes showed statistical discrimination between benign tumor and malignant tumor. LOH of p16, Rb, E-cadherin and p53 TSGs was detected in 36%, 26%, 54% and 60%, respectively. LOH of p16 and Rb genes inversely correlated with tumor grade 1. Low LOH detection rate on E-cadherin gene was measured in T1 tumor and stage I. LOH of p53 gene correlate well with the tumor size and stage. The LOH-High results correlate well with the tumor size and stage.

Conclusion: These results suggest that LOH of the 4 major TSGs may contribute to the development and invasion of IDCs. Also combined use of various LOH markers may help in deciding prognosis of IDCs.

Microsatellite Instability in Invasive Ductal Carcinomas

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Purpose: Recently, microsatellite alterations, especially microsatellite instability (MSI) and LOH, have been postulated as a novel mechanism of carcinogenesis and as a useful prognostic factor in several gastrointestinal malignancies. LOH is related to the allelic loss of various tumor suppressor genes. MSI has been found to be the result of erroneous DNA mismatch repair system and to be involved in the carcinogenesis of the hereditary non-polyposis colon cancers and some portion of sporadic GI cancers. But, study on MSI has been rarely studied in invasive ductal carcinoma. Our objectives were to evaluate MSI and p53 expression in invasive ductal carcinomas.

Methods: MSI analysis was performed by using polymerase chain reaction with five microsatellite markers (BAT25, BAT26, D2S123, D5S346, D17S250 loci recommended in 1998 NCI Workshop on Microsatellite Instability and RER phenotypes) in 50 surgically resected tumors and each non-tumorous counterpart. The p53 expression was studied using immunohistochemistry.

Results: MSI and p53 expression were detected in 22% and 54%. MSI was more frequently detected in tumor grade I, T-stage I, non-metastatic tumor and tumor stage I. Also there are rare cases showing high grade and stage with metastasis in MSI-high group, in which more than 3 microsatellite loci had MSI. p53 expression results correlated well with higher tumor grade. Correlation between MSI and p53 expression was not recognised.

Conclusion: These results may suggest that MSI may be involved in some portions in mammary carcinogenesis and tumor invasion. Also clinical use of MSI status may help in determining the better prognosis among invasive ductal cancer patients.

Patient Responses for Cancer Genetic Counseling in Korea

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Purpose: 1. Compare the knowledge level on the HBOC following genetic counseling. 2. Contribute to nursing education related to hereditary breast cancer and the accumulation of data for genetic counseling in Korea. 3. Research Design: Comparative survey.

Methods: Counseling group 1: BRCA (+), 45 woman Counseling group 2: BRCA(-), 45 woman Control group: 45 woman.

Results: The average of knowledge about the risk of hereditary breast cancer was fourteen point seven five plus minus four point o eight. Sixteen point seven one plus minus two point nine eight for counseling group 1, fifteen point nine one plus minus two point nine o for counseling group 2, eleven point six two plus minus four point two six for control group. So the BRCA positive group had the highest score and the control group had the lowest score. This result had the critical differences. The differences of scores among groups resulted in the education such as, the concept of hereditary breast cancer, the merits and demerits of genetic tests, the meaning of BRCA factor, the effect to family members depend on the genetic tests result and the method of early examination and prevention, before they sign the permission for the genetic tests. And there was no difference between BRCA positive group and BRCA negative group.

Conclusion: 1. Counseling groups understand more of the knowledge about hereditary cancer than non-counseling group. 2. No difference between BRCA positive group and BRCA negative group in the knowledge about hereditary breast cancer because both groups and counseled.

The CHEK2 1100delC Mutation in Korean Patients with Breast Cancer

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Purpose: The sequence variant in the cell cycle checkpoint kinase 2 (CHEK2 1100delC) is a low penetrance breast cancer susceptibility allele, frequently observed in patients with family history of breast cancer and/or young age and the frequency varied according to race or ethnicity. We evaluated the significance of CHEK2 1100delC in predisposition to breast cancer by assessing its frequency in a material of 493 Korean breast cancer patients.

Methods: Four hundred and ninety three Korean patients with breast cancer from the two university hospital were selected for this study. Of the 493 patients entered for this study, 273 were early-onset and/or bilateral, 169 family history of breast cancer. Mutation detection of CHEK2 1100delC was based upon analysis of primer extension products generated for previously amplified genomic DNA using a chip based MALDI-TOP mass spectrometry platform (Sequenom, Inc., CA). After overall measurement automatically, assays which had bad peaks were checked again manually.

Results: None of the 493 Korean patients with breast cancer carried the 1100delC mutation, observed in Caucasians with family history of breast cancer and early-onset breast cancer, with limited frequency.

Conclusion: Previously we observed higher or comparable prevalence of BRCA1 and BRCA2 mutations. In our present study, we evaluated role of CHEK2 1100delC as a susceptibility mutation of breast cancer in the Korean population. However our results suggest that this mutation is absent or may be very infrequent in Korean patients with breast cancer who have high risk of BRCA1 and BRCA2 mutation, making its screening irrelevant from the practical point of view.

CASP8 Polymorphisms, Estrogen and Progesterone Receptor Status, and Breast Cancer Risk

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Purpose: This study was conducted to evaluate the potential role of CASP8 genetic polymorphisms in the etiology of breast cancer in a case-control study, Korea.

Methods: Incident breast cancer cases confirmed histologically (n=1,599) were recruited from two hospitals in Seoul during 2001-2005. Control subjects (n=1,536) were selected from the Health Examinee Cohort from Seoul and Gyeonggi Province surrounding Seoul, Korea. Three SNPs (D302H, 5'-UTR C>T, and K337K G>A) were genotyped by the primer extension assay. The CASP8 D302H, which was not polymorphic in 48 samples, was excluded in further genotyping. Odds ratios and 95% confidential intervals (95% CIs) were estimated by unconditional logistic regression model adjusted for age at enrollment, education, age at first full-term pregnancy, cigarette smoking, and family history of breast cancer.

Results: The 5'-UTR T allele containing genotypes (CT/TT) were associated with an increased risk of breast cancer, compared with those with the CC genotype (OR=1.13, 95% CI=0.95-1.34; and OR=1.48, 95% CI=1.04-2.10, respectively; p-trend=0.02). When stratified by the ER and PR status, the association between the 5'-UTR T allele and breast cancer risk was prominent in ER(+) and PR(+) cases among pre-menopausal women (OR=1.31, 95% CI=1.00-1.72 and OR=1.40, 95% CI=1.06-1.85, respectively), whereas the association was found prominent in ER(-) or PR(-) cases (OR=1.32, 95% CI=0.93-1.87 and OR=1.42, 95% CI=1.04-1.94, respectively) among post-menopausal women.

Conclusion: Our results thus suggest that the CASP8 5'-UTR C>T are associated with breast cancer risks and the effect may be modified by estrogen and progesterone receptor status.

Large-Scale Evaluation of Candidate Genes Identifies Association between FCER1A, OR10J3 and Breast Cancer Risk

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Purpose: This study was conducted to evaluate of common variation in candidate genes for breast cancer risk among Korean women.

Methods: The Illumina GoldenGate assay was used to genotype 1,536 SNPs in 205 genes in a matched case-control study (n=209 sets) in Korea. All SNPs chosen for this platform were drawn from the innate immunity-related genes as previously evaluated in relation to cancer risk or those with evidence for functional significance. We performed gene-based and SNPs based tests evaluating the robustness of our results with FDR and Permutation methods.

Results: FCER1A (rs7548864) and OR10J3 (rs2494251) SNPs were observed strongly associated with breast cancer risk after multiple testing adjustments (global p=0.049). Two SNPs were also associated with increased risk for breast cancer (odds ratio (95% CI): 2.33 (1.48-3.66), 2.09 (1.42-3.09), respectively). Gene-based analyses firstly showed a significant finding in OR10J3 (p for likelihood ratio test, 1 degrees of freedom (df) = 2×10^{-5}). The FDR-adjusted p-value for the association of OR10J3 with breast cancer risk was also significant (global p=0.005 (1 df), p=0.018 (2 df)). Individual SNP-based analyses were quite concordant with gene-based analyses. These two SNPs are adjacently located on chromosome 1q23 which is yet well unknown the functional association with cancer risk.

Conclusion: The FCER1A and OR10J3 have identified the association with breast cancer risks on high throughput SNP technology. Further second stage studies are required to confirm these findings, as well as to examine the biological mechanisms for the associations.

Rare Variant of Hypoxia-Inducible Factor-1A (HIF-1A) and Breast Cancer Risk in Korean Women

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Purpose: Hypoxia inducible factor 1 alpha (HIF1A) is activated by low oxygen condition tension, a key regulator of the gene involved in the cellular response to hypoxia. To evaluate the potential role of genetic polymorphisms of HIF1A in the etiology of breast cancer, a case-control study was conducted in Korea.

Methods: Histologically confirmed incident breast cancer cases (n=1,599) were recruited from two hospitals in Seoul during 2001-2005. Control subjects (n=1,536) were selected from the cohort of health examinees recruited in Seoul and Incheon, Korea. Genotypes of the two polymorphisms (rs11549465: 1772C>T, P582S; rs2057482: Ex15+197C>T, 3'UTR) were determined by the primer extension assay. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated by unconditional logistic regression adjusting for age and history of breast cancer in 1st degree relatives.

Results: Two selected SNPs (Ex15+197C>T and P582S) were not associated with overall breast cancer risk (TT vs. CC: OR=0.9, 95% CI=0.61-1.48, Ser/Ser vs. Pro/Pro: OR=5.5, 95% CI=0.66-45.4, respectively). On the other hand, a significant association between Ser/Ser genotype at codon 582 and breast cancer risk was found among women with larger tumor size (>2 cm) (OR=10.1, 95% CI=1.13-91.1) or without lymph node involvement (OR=9.3, 95% CI=1.08-79.4), though confidence intervals were wide.

Conclusion: Our finding supports the HIF-1 α P582S variant may be a functionally significant prognosis factor in breast carcinogenesis. However, further study is warranted due to low statistical power caused by very low minor allele frequencies.

Interleukin-1 Alpha Gene and Breast Cancer Risk: Candidate-Gene Association Study for 1,536 SNPs

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Purpose: We conducted a large-scale association study evaluating 1,536 SNPs in 264 genes selected for a potential role in breast cancer development to identify specific genes with a role in breast cancer risk among Korean women.

Methods: We evaluated 1,536 common variants of the Non-Hodgkin Lymphoma (NHL)-related genes in a matched case-control study with an Illumina GoldenGate assay. Incident breast cancer cases confirmed histologically (n=209) were recruited from Seoul National University Hospital during 2002-2004. Control subjects (n=209) were selected from the cohort of health examinees recruited in Seoul and Gyeonggi-do, Korea. We performed gene-based and SNP-based tests evaluating the robustness of our results with FDR.

Results: The most significant finding was in the 3' UTR of IL1A (rs2856836, Ex7-592T>C). Gene-based analyses showed a significant finding in IL1A (p for likelihood ratio test, 1 degrees of freedom (df) = 8.1×10^{-7}). The FDR-adjusted p-value for the association of IL1A with breast cancer risk was also significant (global p=0.0002 (1 df), p=0.006 (2 df)). The findings in individual SNP-based analyses were similar to those in gene-based analyses. IL1A (rs2856836) was strongly associated with breast cancer risk after multiple testing adjustments (global p=0.002) and was at increased risk for breast cancer (odds ratio (95% CI): 3.14 (1.90-5.19)).

Conclusion: This large-scale evaluation of candidate cancer genes identified common genetic variants in the regions of IL1A. Further study is needed to support these findings with the mechanisms for the observed associations.

Proposal for Using an International Unified Draft for Chemotherapeutic Regimen Time Schedule Table: ‘Chemo Box’

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Purpose: Chemotherapy used in the current anti-cancer treatment consists of many medications and various recipe methods. Many authors and pharmaceutical companies are describing a variety of meanings in their articles and books. And, many cancer societies are announcing leaning toward the standardization of treatments and are providing guidance on the appropriate regimen for various types of cancer in an attempt to increase the effectiveness and quality of treatments. However, authors and cancer societies use their own notations and are yet to standardize any formats to mark the various anti-cancer chemotherapies. In future, combination of methods for administration of treatment can increase further with the development of more anti-cancer medicines. Therefore, means to mark different kinds of anti-cancer medicines and an individual cycle will be necessary.

Methods: The author proposes an anti-cancer chemotherapy notation scheme (called Chemo Box) as a simple table containing standardized notation as shown below for example.

Results: This notation scheme may give direct assistance to patients receiving anti-cancer chemotherapy in addition to hospital staff and medical workers who are involved in the actual treatment process. It may also assist people learning to use the anti-cancer therapy. Many examples are presented to illustrate the usefulness of the proposed notation system.

TAC		mg/m ²	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18			
			1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15
T	Docetaxel	75	█			█			█			█			█			█			█		
A	Doxorubicin	50	█			█			█			█			█			█			█		
C	Cyclophos.	500																					
Day 3 or 4: Prophylactic G-CSF & antibiotics																							

Fig 1. TAC regimen in adjuvant setting

XT		mg/m ²	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25			
			1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15	1
X	Xeloda®	1250 <i>bid</i>	█	█		█	█		█	█		█	█		█	█		█	█		█	█		█	█		█	█		
T	Docetaxel	75	█			█			█			█			█			█			█			█			█			
Xeloda® ; bid on day 1 - 14																														




Fig 2. XT regimen in metastatic setting

Promoting Breast Health among Young College Age Women through Breastival Events on Campus

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Purpose: The age group of 18-23 is ideal to begin establishing good breast health habits, undo the myths about this disease and promote knowledge of the facts.

Objectives: create an interactive event students willingly attend with enthusiasm and demonstrate interest in learning how to improve and maintain good breast health; educate students about at least 8 facts regarding breast cancer; train them in BSE; educate about reconstruction options if diagnosed; education on proactive steps to take to reduce their risk of getting breast cancer; create an event that can be replicated at other colleges; educate about various breast cancer organizations; provide a mechanism for communicating with students to update them on news about breast health/cancer; help to reduce fear of disease; reach a large number of students at once.

Methods: Invited 8 breast cancer organizations who displayed 10 different flash cards (multiple choice and true/false) on breast health and breast cancer. Students visited Breastival booth to answer a question and get breastival card stamped. When their card was filled they were rewarded with 'bobby prizes'.

Results: Over 600 students attended; 347 visited every booth and answered questions; 326 provided email addresses for contact about educational updates and reminders to do BSE; 100% who responded to survey said they would attend a Breastival again. 61% learned something new. Since the program's inception, more than 100 Breastivals have been held nationally and internationally on college campuses.

Conclusion: A highly successful breast cancer awareness educational program that can be and has been easily replicated elsewhere.

The Life Experiences of Women with Mastectomy through Dynamic Imagery Therapy (DIT)

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Purpose: The purpose of this study was to understand women's life experience of breast cancer with mastectomy through DIT. The participants of this research included 15 women, 35 to 50 years of age. These women were out-patients at G University Hospital, who underwent mastectomy and consented to participate in this research. The participants resided in 4 Cities of G province, South Korea.

Methods: The method was designed using the self-disclosed. The data was collected using in-depth, semi-structured interviews. Data were collected at baseline for 6 weeks after post-mastectomy. The participants were asked to describe their feelings during DIT through Leuner's 12 Themes, such as a flower, a green field, a stream, mountains, a house (self-disclosure of the superficial emotion); a forest, an important persons, a rose, a lion, and an ideal self-image (deep emotion); a cave and a volcano (more deep).

Results: The contents of their reactions to the imagery were analyzed by the author and animagery specialist to exclude individual dogmatism, and to get those agreed results through discussion. The findings were classified into 3 phases; Past, Present and Future. The meaning of the self-disclosure extracted by DIT appeared in the Past phase as Repressed Anger, Present phase as Collapsing oneself and in the Future phase as Anxiety related to uncertainty.

Conclusion: DIT can be a most powerful technique to help reach to an unconscious repressed feeling in a short time. Therefore we suggest that the Life experiences of women with mastectomy through DIT may be applied as an effective nursing intervention.

A Study on the Education for Breast Cancer Patients

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Purpose: This study was a descriptive survey of the education for breast cancer patients by measuring nurses' education performances and patients' benefits and level of knowledge about their disease.

Methods: The population for this study was 28 hospitals with their ratio of cancer patients exceeding 1% of the entire patients registered by Korea Central Cancer Registry. Among them, 13 hospitals agreed to the survey of their nurses, while 6 hospitals agreed to the survey of their breast cancer patients. For this study, a questionnaire consisting of 48 items including the demographic variables was used to collect the data from May 12 to June 7.

Results: Overall education performance score of nurses was 3.39 ± 0.749 . Major education domains by nurses were self-care, treatment, disease-related information, diet-nutrition, psycho-social care, and sexuality. The barriers of nurses' education performance were shortage of time, insufficiency of material, lack of knowledge and skill, and low understanding of patient. Patients with breast cancer were educated most frequently in the domains: self-care, treatment, diet-nutrition, disease-related information, psycho-social care, and sexuality. Major resource of information was a internet (17.83%), a physician (17.44%), a newspaper and a broadcast (16.28%), other patients (15.5%), materials in hospital (11.24%), family member and friends (9.69%), a nurse (7.75%), a book (3.88%).

Conclusion: Role define of nurse was needed as educator and information provider for patients with breast cancer. Nurses may develop an education program in sexuality and psycho-social care and should expand their role of education in sexuality and psycho-social care.

Estimation of Individualized Probabilities of Developing Breast Cancer for Korean Women

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Purpose: The Gail model was used for counseling and chemoprevention of breast cancer. Because Korean women have different incidence rates and risk factors, the Gail model can not properly estimate the breast cancer risk for Korean women. The author developed a Korean breast cancer risk assessment tool, which would display the absolute breast cancer risks of Korean women.

Methods: A risk model was established from a case-control study of 1,687 cases of invasive carcinoma and 1,238 controls. The risk factors selected were age, family history of the first and second relatives, body mass index, age at the first delivery, breast-feeding and a special test on the breasts. A baseline risk and individual breast cancer risk were calculated by a competing risk analysis.

Results: The risk assessment tool was developed in the Internet web page, <http://home.dankook.ac.kr/breast/brc/brc-e.htm>. It calculated the relative risk and the estimated absolute risks following 5, 10 years and up to age 64, 74. The estimated risks of Korean women using this tool were less than the result of NCI risk assessment tool. The risk of breast cancer was highest in the age of forties.

Conclusion: A web-based breast cancer risk assessment tool was developed for Korean women. This program would be useful for the assessment of individual breast cancer risks, the selection of screening tools and preventive options of risk reduction.

Cultural Perspectives on the Female Breasts and Breast Cancer among Korean American Women

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Purpose: Breast cancer threatens the health of both women in the U.S. and Korea representing the most common female cancer in both countries. No research to date has explored women's perceptions on the female breasts and breast cancer inductively which could compose their underlying health beliefs towards the performance of breast cancer screening. The purpose of this study was to explore and describe the perceptions on the female breasts and breast cancer among Korean American women (KAW).

Methods: The grounded theory methodology guided this study. Twenty KAW were recruited for two consecutive individual interviews through a Korean community church in Philadelphia. Using semi-structured questions, the interviews lasted one to two hours in Korean. Recorded and transcribed interviews were analyzed via open-coding, axial coding, and theoretical and selective sampling. The first level coding was conducted in Korean in order not to lose linguistic verbatim and cultural nuances in Korean.

Results: Overriding theme on the female breasts was "relating to loved ones," and "detaching her from her social roles by cutting off a breast" for breast cancer, which demonstrated KAW's collectivistic perspective and cultural values on relationship. Three sub-themes, "reminding her roles in relation to baby and man," "reflecting social desires," and "being treated in culturally appropriate ways" were derived regarding the female breasts.

Conclusion: Much of culture-nuanced perspectives revealed KAW's in-depth perceptions on the female breasts and breast cancer, which would shed lights on developing culturally competent intervention for KAW to improve their screening performance rates.

Risk Factors of Breast Cancer in Women with Metabolic Syndrome

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Purpose: The prevalence of metabolic syndrome has increasing, along with prevalence of breast cancer in Korean women, as lifestyles were westernized. Lifestyle factors as well as heredity have been evaluated as potential contributors to these two diseases. Several studies reported increased insulin and low HDL in metabolic syndrome as being casually linked to breast cancer. The purpose of the current study was to identify the distribution of risk factors of breast cancer in women with metabolic syndrome.

Methods: The participants were 149 women with metabolic syndrome categorized by NCEP ATP-III, aged between 40-59 who registered at the Life Long Health Center in two cities. Data were collected using questionnaires comprising age, family history of breast cancer, breast disease history, pregnancy history, number of children, breast-feeding, age at menarche and menopause, BMI, smoking, alcohol, diet, and exercise.

Results: More than half of the samples (51.7%) were over 50 years old. Most prevalent risk factor was no exercise (72.3%); and once more meat consumption per week (60.4%), below two children (56.4%), BMI ≥ 26 (48.3%), alcohol (18.6%), respectively.

Conclusion: The results showed that women with metabolic syndrome had modifiable risk factors of breast cancer such as lack of exercise and obesity. Based on these results, effective and tailored interventions to prevent breast cancer for women with metabolic syndrome should address controlling weight and encouraging exercise.

Clinical Characteristics and Prognosis of Breast Cancer in Very Young Korean Women

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Purpose: There are only few reports about breast cancer in very young women under 25 years. The purpose of this study was to evaluate the clinicopathological characteristics and the prognosis of breast cancer in women age 25 year or less.

Methods: 3,812 female breast cancer patients, treated at the Asan medical center from January 1992 to December 2002, were reviewed retrospectively. We investigated the clinicopathological characteristics and the prognosis of 25 year old or younger breast cancer patients. Results were compared with the counter age(>25) group and age 26-35.

Results: Twenty-five cases were examined, with a median follow-up of 47 months. A median age was 24 years. Two patients had ductal carcinoma in situ (DCIS), one patient had Lobular carcinoma in situ (LCIS) while 19 patients had invasive carcinomas. A breast conserving surgery was performed on 12 out of 25 patients (48%). Axillary nodal metastases were present in 10 out of 25 patients (40%). Of the 19 cases of invasive disease, 4 out of 13 patients (21%) experienced recurrence and two patients died of breast carcinoma. There was no difference in overall survival between the patients aged 25 year or less and those aged 26-35. There was no significant difference in clinicopathologic characteristic between the very young and the young, except the mean age of menarche (13.8 ± 0.95 vs. 14.3 ± 1.4 ; $p=0.006$).

Conclusion: Our study suggest that although there was difference between older women with breast carcinoma, there was no difference in prognosis and clinicopathologic characteristics between the very young and the young.

Clinicopathological Features of Women Age ≤ 35 Years old Diagnosed with Invasive Breast Cancer in Brunei Darussalam

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Purpose: A young age at diagnosis of Breast cancer is associated with biologically more aggressive cancer. There is however few published data in the Asian population. The purpose of this study was to look at the clinical presentation, pathologic findings, tumor characteristics and outcome for women age 35 or less diagnosed with invasive breast carcinoma.

Methods: A retrospective study was conducted of women diagnosed with invasive breast carcinoma from January 1998 to June 2007. Staging was done according to AJCC staging. Histological grade, presence of hormone receptors and HER2 expression by immunohistochemistry.

Results: A total of 37 women age 35 or less were diagnosed with breast cancer during this period. The mean age of the patient was 31 (21-35). 11% had family history of breast cancer, 8% were diagnosed during pregnancy and one patient has Poland's syndrome. Patients were staged at: 7 stage I, 12 stage II, 10 stage III, 7 stage IV and in 1 staging was not available. Histologically, majority (83%) were ductal carcinoma. More than half of patients (56%) who underwent axillary lymph node dissection had positive lymph nodes at diagnosis. 57% did not express any hormonal receptor positivity. Her2 3+ and grade 3 was observed in 46% and 51% respectively. With a median follow up of 42 months, there were 8 deaths, 2 relapses and 2 patients developed contra-lateral breast cancer.

Conclusion: This young population of breast cancer patients appears to have a more aggressive tumor with a higher proportion of patients expressing HER2 3+, high tumor grade and hormonal receptor negativity.

Comparison of Body Mass Index between Hypo- and Macro-Mastia

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Purpose: This study was performed under a hypothesis that women with small breasts or large breasts should differ from each other not only in size of breasts but also body habitus, due to differences in body fat distribution and physical activity.

Methods: During the period from Jan. 2002 to Jun 2006, four hundreds sixty one patients with hypomastia and one hundred four patients with macromastia visited M.D. Clinic, Seoul, Korea. They were divided into three groups (Group 1; underweight BMI <18.5, Group 2; normal BMI 18.5-22.9, Group 3; overweight BMI ≥23) according to Body Mass Index (BMI).

Results: Average age of women with hypomastia and macromastia were 32 and 34.5 respectively. Average BMI was 18.88 in hypomastia group and 22.19 in macromastia group ($p < 0.001$). In hypomastia group, distribution of BMI was group 1: 44.5% (n=205), group 2: 53.8 (n=248), group 3: 1.7% (n=8). However, in macromastia group, higher proportion of overweight was observed; group 1: 7.7% (n=8), group 2: 71.1% (n=32), group 3: 27.3 (n=3). In hypomastia group, group 3 were 0 in twenties, 0.9% (n=2) in thirties, 6% (n=3) in forties and 27.3% (n=3) in fifties, but in macromastia group, group 3 were 17.8% (n=8) in twenties, 32% (n=8) in thirties, 50% (n=12) in forties and 100% (n=10) in fifties.

Conclusion: BMI of women with macromastia was significantly higher compared to women with hypomastia. Although increase of BMI was observed as the age advances in both groups, women with macromastia seem to have strong tendency to become obese with ageing.

Breast Cancer in the Elderly: Histological, Hormonal and Surgical Characteristics

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Purpose: The age of the general population in the western world is steadily increasing. Since in 1980 11.3% of the entire population reached 65 years of age, it is estimated that in 2030, 20% of the population will reach 75 years of age. In order to understand better the nature of breast cancer in the elderly, we compared the biological characteristics of breast cancer patients, and the surgical therapy of patients aged 70 years and older, with those of younger patients who were treated in our Medical Center.

Methods: This was a retrospective study of all patients diagnosed with breast cancer at the Kosin medical center, between June 2000 and March 2004. The patients were interviewed and a personal questionnaire regarding personal and menstrual history was filled out. All available clinical data were collected and entered into a database. Patients were divided into two groups: less than 70 years of age (group A), and more than 70 years of age (group B).

Results: There was no difference in stage, size, state of axillary nodes, grade, histological types, Ki-67, vascular invasion, estrogen receptor rate, and HER-2/neu (+) rate. Positive estrogen receptor rate was higher in older patients (58% vs. 69%). Tumors were larger ($p=0.01$) and their stage higher ($p=0.024$) in patients more than 80 years of age.

Conclusion: We conclude that breast cancer characteristics and menstrual risk factors are similar in the two age groups.

Polymorphic Analysis of MHC-Linked Heat Shock Protein 70 (Hsp70-2 and Hsp70-hom) Genes: Their Susceptibility and Prognostic Implications in Breast Carcinoma

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Purpose: Heat Shock Proteins (Hsp) are expressed at high levels in wide range of tumors. They are determining factors for tumor cell survival as they promote autonomous cell proliferation, inhibit cell death pathways, and delay senescence as well as influence the immune response to tumor cells.

Methods: Polymerase Chain Reaction and restriction enzymes were utilized to characterize the frequency of two polymorphisms within Hsp70-2 and Hsp70-hom genes in 114 breast carcinoma cases and 90 healthy controls in order to characterize the association of its genotypic variants in predisposition to and clinical outcome of breast carcinoma patients from Kashmir. Association of high frequency variants of Hsp70 genes with various clinicopathological features of prognostic significance was assessed by χ^2 test using SPSS software.

Results: In the present study, allelic frequency of Hsp70-2 A/G heterozygote (0.88) was found to be significantly high in breast carcinoma cases compared to control (0.744) ($p=0.008$, $RR=2.67$). Similarly, significantly high frequency of 0.50 (vs. 0.3 in control) of Hsp70-homC/C allele was found in homozygous condition in breast cancer cases, suggestive of positive relative risk associated with this genotype ($RR=2.42$, $p=0.003$). The overall genotypic frequency data analysis of Hsp70-2 and Hsp70-hom genes was significant ($\chi^2=11.46$, $p=0.003$; and $\chi^2=10.56$, $p=0.005$).

Conclusion: These results suggest Hsp70-2 A/G or G/G and Hsp70homC/C as risk imposing haplotype in our population. The study, therefore, suggests Hsp70-2A/G or G/G and Hsp70homC/C genotypes as potential susceptibility markers and independent prognostic indicators in breast carcinoma patients.

Differences in Recurrent Genomic Alterations between the Molecular Subtypes of Breast Cancer

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Purpose: We aimed to identify the pattern of genomic copy number alterations in breast cancer, characteristic to molecular subtype of breast cancer.

Methods: Frozen tissues obtained from 116 primary invasive breast cancer patients were used for high-resolution array comparative genomic hybridization with 4,045 BAC clones. The classification of subtype was based on immunohistochemistry results.

Results: Sixty-two cases were luminal, 23 were HER2+/ER-, and 29 were Basal-like subtype. The average number of altered clones was highest in basal-like subtype and lowest in HER2+/ER- subtype. Recurrent gains common to all subtypes were 1q23-q32, 8p12-p11, 8q21-q24, 13q34, 16p13, 20q13, and 22q11. Recurrent gains found only in ER- tumors were 5p15, 7p22, and 7q36. A recurrent gain region found only in luminal subtype was 11q13.3 (CCND1, FGF3). Many recurrent gains were found exclusively in basal-like subtype: 3q29, 9p24-p23, 9p13, 10p15-p14, 10p12, 10q26, 12p13, 12q24, 15q26, 17q24-q25, 17q25, 18q23, and 21q22. Recurrent losses common to all subtypes were 8p23, 10q11, and 14q32. A recurrent gain found only in ER- tumors was 5q13. A recurrent gain region found only in basal-like subtype was 5q23. Recurrent losses found only in luminal subtype were 11q23, 13q14-q21, 16q21-q22, and 16q23-24. Cadherins 5, 11, and 13 were located in these 16q regions.

Conclusion: We found many gain and loss regions characteristic to the three molecular subtypes. Many of the regions coincided with previous CGH array studies. Novel recurrent altered regions especially gains in basal-like subtype and losses in luminal subtype were interesting to us and under validation.

Increased Expression of RhoGDI-2 in Breast Cancer is Associated with Shorter Disease-free Survival

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Purpose: Rho GTPases are key molecules in tumor cell invasion and metastasis, and Rho guanine dissociation inhibitor (RhoGDI) regulates Rho GTPase activity. The exact role of RhoGDI-2 in cancer cell biology is unclear. RhoGDI-2 has been known to be a metastasis-suppressor gene in various types of tumors. However, in recent studies, RhoGDI-2 promoted breast cancer cell invasiveness. Although demonstrated only in vitro, the pro-metastatic and pro-invasive properties of RhoGDI-2 in breast cancer cells are contradictory to the previous reports.

Methods: We have recently reported the lists of up-regulated proteins in breast cancer tissues. Among the up-regulated proteins, RhoGDI-2 showed prominent up-regulation. To verify these preliminary findings, we performed proteomic analysis in 12 patients using 2-DE and MALDI-TOF. Altered expression of RhoGDI-2 was confirmed by western blotting. Subsequently, to investigate its clinical significance, we performed immunohistochemical staining against RhoGDI-2 using 86 paraffin-embedded surgical specimens.

Results: Cancerous and non-cancerous breast tissues of 12 patients were used for proteomic analysis. RhoGDI-2 showed significant up-regulation in cancerous tissues ($p=0.019$), which was subsequently confirmed by western blotting. Immunohistochemical staining showed that RhoGDI-2 expression did not show any significant change according to tumor size, lymph node metastasis, hormone receptor status, or tumor invasiveness. However, RhoGDI-2 expressing tumors showed significantly shorter disease-free survival than RhoGDI-2 negative tumors ($p=0.017$).

Conclusion: Our result supports the pro-metastatic role of RhoGDI-2 in breast cancer expression and is concordant with the pro-invasive properties of RhoGDI-2 demonstrated in the in vitro studies using breast cancer cell lines.

Performance Status and Single Brain Metastasis were Significant Factor for Survival in 198 Metastatic Breast Cancer Patients with Brain Parenchymal Metastasis: Single Center Experience

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Purpose: The purpose of this retrospective study is to analyze the overall survival of patients with brain metastases from breast cancer and to identify prognostic factors affecting clinical outcome.

Methods: Of the 7,872 patients histologically diagnosed with breast cancer between January 1990 and July 2006 at Asan Medical Center, 198 patients with solitary or multiple brain metastases were included in this retrospective study.

Results: The median age of the patients at the diagnosis of brain metastases was 45 years (range, 26-78). Fifty-five patients (28%) had a single brain metastasis, whereas 139 (70%) had more than two. Whole brain radiation was administered to 157 (79.2%) patients. Seven (3.5%) patients underwent resection of solitary brain metastases, 22 (11%) patients underwent gamma-knife, and 9 (4.5%) received no treatment. The overall median survival time was 5.6 months (95% CI, 4.7-6.5 months) and 23.1% of the patients survived more than 1 year. The median overall survival time of patients treated with WBRT was 5.4 months, 14.9 months in patients treated with surgery or gamma-knife, and 2.1 months in no treatment group, respectively ($p < 0.001$). Multivariate analysis demonstrated that ECOG performance status (RR=0.594, 95% CI 0.409-0.864, $p=0.006$), and number of brain metastases (RR=0.685, 95% CI 0.463-1.014, $p=0.05$) were independent factors associated with survival. Treatment modalities (RR=1.582, 95% CI 0.955-2.622, $p=0.07$) were of borderline significance.

Conclusion: Performance status, number of brain metastases and treatment modalities were significantly associated with survival. The characteristics of initial primary breast lesions did not influence the survival after brain metastasis occurred.

E-cadherin Gene Alterations in Invasive Ductal Carcinoma

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Purpose: E-cadherin gene, located on chromosome 16q22, may play principal roles for cell adhesion, and loss of E-cadherin expression is found in various cancers. The E-cadherin gene alterations including gene mutation, loss of heterozygosity (LOH), DNA hypermethylation and protein expression loss have been rarely studied in mammary carcinogenesis. This study aimed to do comprehensive approach to E-cadherin gene alterations in invasive ductal carcinoma and to correlate them with various clinicopathological factors in 50 cases of surgically resected breast cancer.

Methods: The LOH analysis was performed by using polymerase chain reaction with three polymorphic microsatellite markers (D16S419, D16S3106, D16S498) in 50 surgically resected tumors and each non-tumorous counterpart. The E-cadherin protein expression was studied using immunohistochemistry.

Results: LOH and loss of protein expression were detected in 54% and 46% of the tumors, respectively. Neither LOH nor protein loss were detected in non-tumor lesions. LOH results correlated well with tumor size and lymph node metastasis. Protein loss results correlated well with the histological grade of tumors. Correlation between LOH and protein loss was not recognized.

Conclusion: These results suggest that E-cadherin LOH may be associated with tumor metastasis and tumor progression. E-cadherin protein loss may be related with the dedifferentiation in some portions of invasive ductal carcinomas. We propose E-cadherin LOH and protein loss may contribute to tumor progression by independent mechanism.

Targeting Downstream or Epigenetic Modulation of HER-2 Signaling Increased Radiosensitivities of Human Breast Carcinoma Cells: Alternative Strategies for Therapeutic Resistance

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Purpose: Despite of the solid evidences regarding the potential value of targeting HER-2 signaling to enhance the anti-tumor activity of radiation, therapeutic resistance has been emerged as an important issue. We tried to identify possible approach to tackle this issue that may limit therapeutic benefit of HER-2 targeted therapy combined with radiation.

Methods: We evaluated the inhibitors targeting downstream signaling of HER-2 and histone deacetylase (HDAC) inhibitor LBH589 (Novartis, U.S.A.) if they would radiosensitize a panel of breast cancer cells with different HER-2 status by clonogenic assay. Mechanistic role of HDAC 6 isotype was investigated using RNA interference and ectopic overexpression of cDNA.

Results: Selective inhibition of PI3K-Akt-mTOR pathway components using pharmacologic inhibitors (LY294002, Akt1 inhibitor VIII, Rapamycin) significantly attenuated p-Akt, p-70S6K, and p-S6 ribosomal protein expressions and showed modest radiosensitization of SKBR3 cells. Histone deacetylase inhibitor, LBH589 significantly enhanced the radiosensitivity. Abrogation of radiation induced G2/M arrest, prolonged γ H2AX foci, aberrant mitotic features and increased apoptosis were usual findings. LBH589 increased acetylation of histone H3, tubulin and also increased acetylation of HSP90 which was associated with ubiquitination and downregulation of level of client oncoproteins Her-2, c-raf-1, p-Akt and p-MAPK. Specific inhibition of HDAC6 isotype by RNAi increased acetylation of HSP90 reduced the chaperone association with client proteins and increased radiosensitivity. Ectopic overexpression of HDAC6 led to partial rescue from LBH589 mediated radiosensitization for HER-2 activated cells.

Conclusion: Taken together, these results suggest possible mechanisms to counteract the HER-2 prosurvival signaling which is implicated in radioresistance, and propose the alternative strategies to overcome therapeutic resistances of available HER-2 inhibitors.

Docetaxel-induced Apoptosis of Human Umbilical Vein Endothelial Cell (HUVEC) is Mediated by Activation of Caspases, Mapk, ERK1/2 and P38

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Purpose: In this study, our aims were: (i) to evaluate the apoptotic activity of docetaxel in HUVEC; (ii) to examine the role of Bcl-2 family proteins (Bcl-2, Bax), poly-caspases and MAPK signal pathway (iii) to define the proposed mechanism of apoptosis by docetaxel in HUVEC.

Methods: HUVECs were plated into 96 well plate at a concentration of 1×10^3 per well. After 72 hrs, the cells were treated with docetaxel at the indicated concentration for 48 hrs. Cell viability was determined using cell counting kit-8. Caspase activation assays were done with apoptosis detection kit specific for activity of the poly-caspases. And western blot analysis was also performed with specific primary Abs [ERK1/2, phospho-(Thr202/Tyr204)-ERK1/2, p38, and phospho-(Thr180/Tyr182)-p38].

Results: The IC₅₀ of HUVEC cells treated with docetaxel was 1.0 nM and docetaxel inhibited the proliferation of HUVEC cells in a dose-dependent manner. Cells with active caspases retain the FLICA substrate and fluorescence. Caspase activity was not seen in medium-treated control cells. But caspase activity was increased with the dose dependent manner of docetaxel, from 0.5 nm to 100 nm. Docetaxel caused time and concentration dependent phosphorylation of both ERK1/2 and p38. Bax/Bcl-2 ratio in HUVEC was increased by time and dose dependent manner.

Conclusion: Caspases and MAPK signaling pathways play an important role in the regulation of docetaxel induced apoptosis in HUVECs. Docetaxel could be an effective chemotherapeutic agent in the treatment of breast cancer by inducing anti-angiogenic effects.

Ellagic Acid Shows Different Anti-Proliferative Effects between MDA-MB-231 and MCF-7 Human Breast Cancer Cell Lines

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Purpose: Ellagic acid has been demonstrated that it can inhibit tumor growth. However, the mechanism that ellagic acid elicits the anti-proliferative effect is poorly understood. Our objective in this study was to evaluate the biological activity of ellagic acid by comparing the anti-proliferative effect and apoptotic pathway of ellagic acid between human breast cancer cell lines.

Methods: As cell models, MCF-7 and MDA-MB-231 human breast cancer cell lines were used. Anti-proliferative effect was evaluated using MTT assay. Cell cycle was analyzed by flow cytometry. Western blotting was performed to show expressions of bcl-xL, cytochrome c and survivin.

Results: The ellagic acid in MDA-MB-231 cells showed significant anti-proliferative effects with dose dependent pattern. The anti-proliferative effects in MCF-7 cells were observed in only high concentration. Ellagic acid has no effect on cell cycle in both breast cancer cells. In MDA-MB-231, expression of bcl-xL was decreased with the decreasing of concentration of ellagic acid. And the expression of cytochrome c in cytosol was increased with decreased expression of bcl-xL. Ellagic acid also decreased the expression of survivin. In MCF-7, expressions of bcl-xL and cytochrome c showed no change after treatment of ellagic acid, even in high dose.

Conclusion: Ellagic acid has anti-proliferative effect in MDA-MB-231 cells. This effect of ellagic acid is through the intrinsic pathway in MDA-MB-231 cells. However, the expression of bcl-xL showed no change in MCF-7 cells. Ellagic acid has different anti-proliferative effect between human breast cancer cell lines.

The Role of NF- κ B in Osteolytic Bone Metastasis of Breast Cancer Cells

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Purpose: The incidence of breast cancer is on the rise in Korea and United States, and the prevalence of this human malignancy is very significant by the fact that 70% of the women who die from breast cancer show metastasis to bone. However, the bone biology of the development of this tumor is still poorly understood.

Methods: MDA-MB-231 cells were cultured in DMEM supplemented with 10% FBS (Invitrogen). The full-length cDNA clone for human CSF2 was subcloned into pBabe-puro retroviral vectors. Retroviral infections were performed as described elsewhere previously. Serial tissue sections from human bone-metastatic tumors were provided by University of Michigan and Henry Ford Health System. Breast cancer cells (105/100 μ L PBS) were injected into the left cardiac ventricle in 5-week-old immunodeficient mice. Radiographs were taken using a Faxitron MX-20 X-ray machine (Faxitron X-ray). Then serial sections were prepared and stained with hematoxylin and eosin.

Results: We investigated that constitutive nuclear factor- κ B (NF- κ B) induces granulocyte macrophage-colony stimulating factor (GM-CSF) in breast cancer cells to stimulate osteoclast formation of bone marrow cells, which plays an initiating and critical role in activating vicious cycle of osteolytic bone metastasis followed by the increased destruction of large amount of bone at the site of the tumor growth in vivo. Moreover, we found that the expression of GM-CSF correlated with NF- κ B activation in human bone-metastatic tumor tissues.

Conclusion: NF- κ B in breast cancer cells promotes osteolytic bone metastasis by inducing osteoclastogenesis through GM-CSF.

Quantitative Promoter Hypermethylation Profiles of Ductal Carcinoma In Situ in American and Korean Women: Potential Applications for Diagnosis

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Purpose: We examined the prevalence of methylation in breast ductal carcinoma in situ (DCIS) samples from American and Korean women in an effort to reveal geographic difference. We also investigated the diagnostic potential of DNA methylation-based markers in tissue samples of DCIS.

Methods: Quantitative multiplex methylation-specific PCR (QM-MSP) of ten genes (APC1, BRCA1, BRCA2, CDH1, Cyclin D2, ER α , HIN-1, RAR- β , RASSF1A, and Twist) was performed on DNA from 52 American and 48 Korean DCIS as well as normal breast tissues.

Results: Methylation levels of APC1, Cyclin D2, HIN-1, RASSF1A, and Twist and cumulative methylation were significantly higher in DCIS than in normal tissues. Statistically significant differences in the levels of methylation between American and Korean DCIS were only found for CDH1 and RAR- β . The differences in methylation frequency in DCIS between the two groups were not statistically significant for any of genes, except CDH1 and ER α . Multigene promoter hypermethylation was a prominent feature in both DCIS groups. With the three-gene panel (APC1, HIN-1, and RASSF1A), QM-MSP distinguished between DCIS and normal breast tissues with a sensitivity of 94 to 96% and a specificity of 80 to 88%.

Conclusion: Our study demonstrated that methylation profiles of DCIS between American and Korean women were significantly different for 3 of 10 genes. Methylation status of a panel of genes measured in a quantitative manner accurately discriminates between normal and DCIS tissues of both groups and may be useful as an ancillary tool for DCIS detection in breast tissues.

The New Theory of Carcinogenesis the Theory of Gene Multiple Hits

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Purpose: In order to find the cancer development mechanism for the best cancer cure and treatment.

Methods: Summarizes the cancer scientific research findings.

Results: Explanation of the gene multiple hits theory: We have known that cancer development is caused by the long time carcinogens' effects. The carcinogens include environmental or chemical factors; biological factors; physical factors and hereditary factors etc. All these factors display complicated effects on human body. After all, the author may say in this way that before the cancer development, there are many different proto-oncogenes and tumor suppressive genes suffer from many different carcinogens' hits and damages. And finally the cancer is developed.

Conclusion: The significances of the new theory are great. The new theory not only fully explains the research findings for cancer development mechanism, but also summarizes lots of different scientific research findings, and using the single new theory represents the whole related scientific research findings. The new theory clearly addresses the cancer development mechanism, which indicates the new theory is a very good one. The gene multiple hits new theory provides the best directive references for the further cancer research, prevention, early diagnosis, early cure and cancer treatment.

A Study for Effect of Peroxisome Proliferator-Activated Receptor-Gamma Agonist, Troglitazone on Estrogen Receptor Positive and Negative Breast Cancer Cells

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Purpose: It is reported that PPAR-gamma (PPAR- γ) agonist could serve as negative regulators of breast cancer development and progression, but their mechanism is still unknown. The purpose of this study was to evaluate the mechanism that PPAR- γ agonist, troglitazone would induce antiproliferative effect on MCF-7 (ER-positive) and MDA-MB-231 (ER-negative) breast cancer cells.

Methods: Cytostatic/cytotoxic effects of troglitazone were measured with mitochondrial tetrazolium (MTT) assay. The cell cycle distribution and apoptosis induction were evaluated by using the flow cytometry. Detection of apoptosis was carried out using a DNA fragmentation assay based on TUNEL staining. For morphological examination of apoptotic changes, cells were stained with Hoechst 33342.

Results: Troglitazone showed antiproliferative effect on MCF-7 breast cancer cells with tamoxifen, respectively and synergically. Troglitazone and tamoxifen could induce cell cycle G1 arrest and apoptosis of MCF-7 cells, through upregulating or downregulating the expression of apoptosis-related genes such as Bax, Bcl-2 and cyclin D1. MDA-MB-231 cells exposed to troglitazone showed G1 arrest as well as induction of characteristic morphological changes of apoptosis. Accumulation of cells in G1 was accompanied by an attenuation of retinoblastoma (Rb) protein phosphorylation associated with decreased cyclin dependent kinase 2 (CDK2) activities. Troglitazone increased the expression of CDK inhibitor, p21 and p27. Apoptosis by troglitazone involves activation of NF- κ B and caspase-3.

Conclusion: PPAR- γ agonist, troglitazone increase the sensitivity of hormonal therapy in MCF-7 breast cancer cells and induce cell cycle arrest and apoptosis in MDA-MB-231 cells. These results suggest that troglitazone has anticancer effect on both ER-positive and negative breast cancer cells.

Association between Promoter Hypermethylation of the p16INK4a and hTERT Genes and their Protein Expressions in Human Breast Cancer

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Purpose: This study was undertaken to observe the pattern of methylation of the p16INK4a and human telomerase reverse transcriptase (hTERT) genes and the p16 and hTERT protein expressions in invasive ductal carcinoma of the breast. In addition, we evaluated the relationship between the methylation status of the two genes and their protein expressions.

Methods: We performed methylation-specific PCR (MSP) and immunohistochemical staining in 63 breast cancer specimens.

Results: There was no statistical association between p16INK4a gene methylation and the histological grade (tumor grade, size, lymph node status). Methylation of the hTERT promoter did show significant differences according to the histological tumor grade and size, but there was no clinical significance. Methylation of the p16INK4a and hTERT genes was found in 22.2% and 31.8% of the specimens, respectively. A negative p16 protein expression (0-10% expression rate) was observed in 38.1% of the specimens (24 of 63). A positive hTERT expression (more than 1 25% expression rate) was observed in 73.0% of the specimens (46 of 63). There was no statistical significance in the relationship between the methylation status and the protein expression.

Conclusion: Our data suggest that methylation of the p16 and hTERT genes is not associated with their protein expressions according to the immunohistochemistry. There seemed to be another complicated mechanism for p16 inactivation and hTERT activation in breast cancer.

TGF-beta1 Regulates Id-1 Expression through PKC-delta in MDA-MB-231 Breast Cancer Cell

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Purpose: Transforming growth factor- β superfamily transduces their signals by activating R-smad and regulates expression of Id protein which plays an essential role in inhibition of differentiation and cell cycle arrest in several cancer cell lines. Here we report that TGF β 1 regulates Id-1 expression through PKC δ signal in MDA-MB-231.

Methods: The level of Id-1 mRNA and protein were determined by Northern blot analysis and Western blot, respectively. Protein-binding sites within the Id-1 promoter region were investigated by DNase I footprinting assay and the binding abilities of CREB/ATF, SBE, and Egr-1 were determined by DNA mobility shift assay.

Results: The level of Id-1 mRNA was transiently increased at 1 hour and rapidly disappeared at 3 hours by TGF β 1. Pretreatment with cycloheximide completely blocked TGF β 1-dependent induction of Id-1 mRNA and the level of TGF β 1-induced Id-1 mRNA level was also reduced by pretreatment of actinomycin-D. In DNase I footprinting analysis, the nuclear factors interacting with the cis-elements were identified in TGF β 1-untreated and -treated MDA-MB-231. The binding of trans-acting factors were not different between control and TGF β 1-treated cells. Phospho-smad2 was slightly increased after TGF β 1 treatment in cytosolic fraction, but it was not detected until 24 hrs in nuclear fraction. Moreover, pretreatment of SB-431542 did not prevent TGF β 1-induced Id-1 expression. The level of TGF β 1-induced Id-1 mRNA was significantly reduced by rottlerin and Ro 31-8220 in dose-dependent manners.

Conclusion: Taken together, these results suggest that TGF β 1-dependent regulation of Id-1 gene expression may be related to PKC δ signaling, smad-independent pathway in MDA-MB-231. (Supported by Korea Research Foundation and Dr. Park's Breast Clinic)

Omega-3 Polyunsaturated Fatty Acids Suppress Cell Proliferation through down Regulation of β -Catenin and Cell Invasion through Reduction of MMP-2 and MMP-9 Activity in Breast Cancer Cells

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Purpose: Omega-3 polyunsaturated fatty acids (ω 3-PUFAs) are known to inhibit the cell growth of human breast cancer, although the molecular mechanisms for their anticancer actions are not fully understood. This study was designed to investigate the possible mechanisms on the suppression of breast cancer cell growth and invasion by ω 3-PUFAs.

Methods: The cytotoxicity of ω 3-PUFAs was investigated by MTT assay and the ratio of cell cycle was determined by FACS analysis. Western blot was performed to determine the level of PARP, beta-catenin and NF κ B. The activities of MMP-2 and MMP-9 were investigated by zymography.

Results: Treatment of breast cancer cells (MDA-MB-231, MCF-7, T47D) with ω 3-PUFAs, DHA and EPA, for 24 hours resulted in a dose-dependent inhibition of cell growth; in contrast, arachidonic acid (ω 6-PUFA), had no significant effect. The observations that DHA increased subG1 population and cleaved form of PARP indicate induction of apoptosis. In addition, DHA treatment progressively reduced the level of beta-catenin protein in MDA-MB-231 and T47D. In gelatin embedded zymography, activities of MMP-2 and MMP-9 were decreased by DHA treatment and Prostaglandin E2-dependent increase of MMP-2 and MMP-9 activity was inhibited by DHA pretreatment. DHA also decreased invasiveness of MDA-MB-231 in a dose-dependent manner.

Conclusion: These results indicate ω 3-PUFAs inhibit cell growth through β -catenin degradation and inhibit cellular invasion through the decrease of MMP-2 and MMP-9 activities in breast cancer cell. Thus, utilization of ω 3-PUFAs may represent an effective and safe therapeutic approach for the chemoprevention and treatment of human breast cancer. (This study is partially supported by Dr. Park's Breast Clinic)

Cross-Linking of CD24 Inhibits Growth of MCF-7 Breast Cancer Cells

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Purpose: The effects of neutralization of CD24 via cross-linking on different aspects of breast tumour biology are yet to be established. We analyzed the impact of cross-linking CD24 on human breast cancer cell lines MCF-7 and MDA-MB-231.

Methods: MCF-7 and MDA-MB-231 were cross-linked with anti rabbit polyclonal IgG or anti-human CD24 rabbit polyclonal antibodies and then proliferated. Changes in cell characteristics such as, cell cycle, degree of apoptosis, survival in three-dimensional cultures, adhesion, and migration ability were assayed in MCF-7 after CD24 cross-linking.

Results: Expressions of CD24 analyzed by flow cytometry in MDA-MB-231 and MCF-7 were 2% and 65%, respectively. After cross-linking CD24 with antibody of 500 ng/mL concentrations, the time dependent reduction in proliferation was shown in MCF-7, in contrast to no change in MDA-MB-231. In MCF-7, survival rate decreased by 15% on MTT assay using three-dimensional culture system by CD24 cross-linking. Increased apoptosis determined through annexin V staining was shown, while there was no cell cycle arrest in CD24 cross-linked MCF-7. The migration capacity of MCF-7 was significantly diminished by 30% after cross-linking CD24.

Conclusion: These results showed that cross-linking of CD24 could inhibit growth and migration in MCF-7. It suggests that CD24 might be considered as a novel therapeutic target for breast cancer expressing this protein.

MDA-MB-231 Cells Cultured on Poly-Hema-Coated Dish are Less Growth of Tumor, yet Show More Invasive, Than Cells Cultured on the Tissue Culture Dish

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Purpose: Most cancer cells grow upon adhesion to membrane including ECM but die without affinity to ECM, and the cell death is named anoikis. However, little has been known about invasiveness and growth of tumor in anoikis-resistant cells.

Methods: MDA-MB-231 was cultured on dishes coated with or without poly-HEMA for a long time. After several passages, we obtained anoikis-resistance cells surviving and proliferating on the poly-HEMA culture condition.

Results: To observe relative cell growth rate between adherent and anoikis-resistance cells, cell numbers were counted 72 h after seeding, and we observed that anoikis-resistant cells addressed decreased proliferation about 50% compared to adherent cells. We also observed invasiveness using matrigel in adherent and anoikis-resistance cells. In contrast to proliferation, anoikis-resistant cells increased invasiveness about 50%. We observed cell cycle, apoptosis using annexin V staining, adhesion ability, expression of beta 1 integrin, expression of FAK-p, and expression of MMP. Cell cycle, apoptosis, and expression of FAK-p are not different. Anoikis-resistant cells showed decreased adhesion ability and expression of beta 1 integrin but highly increased expression of MMP.

Conclusion: We show that anoikis-resistance cells are less growth of tumor but more invasive. Suspension culture system using Poly-HEMA may be a useful method in studying anoikis-resistance cells.

Cross-Linking of CD24 Inhibits Adhesion, Invasion, and Survival of MCF-7 Breast Cancer Cells

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Purpose: Several studies show that CD24 plays important roles in the progression, migration, and metastasis of human breast cancer. However, the effects of neutralizing CD24 via cross-linking on different aspects of breast tumor biology are yet to be established. We analyzed the impact of cross-linking CD24 on MCF-7, an established human breast cancer cell line.

Methods: Expression of CD24 in MCF-7 cells was determined by FACS. After cross-linking MCF-7 with an anti-rabbit polyclonal CD24 (FL-80) antibody (500 ng/mL), viable cells were counted by trypan blue staining. Moreover, the adhesion and invasion abilities of CD24-cross-linked MCF-7 cells were assessed. Cell cycle and apoptosis assays were performed by Annexin V staining followed by flow cytometry.

Results: The expression rate of CD24 in MCF-7 cells was 65%. Following cross-linking of CD24, the number of viable cells decreased markedly in a time- and dose-dependent manner. We observed an 8% reduction in cell adhesion ability at 24 h, and 50% reduction in invasion at 72 h after cross-linking of CD24. While CD24 cross-linking had no effects on the cell cycle, the proportion of Annexin V-stained apoptotic cells increased by 17% at 72 h after treatment. Cross-linking of CD24 inhibited cell adhesion and invasion, and induced apoptosis of MCF-7.

Conclusion: Based on these findings, we propose that CD24 is a novel therapeutic target for breast cancers expressing this protein.

Orthotopic Transplantation for Ectopic Tumor Formation in Nude Mice is More Effective than Heterotopic Transplantation of Estrogen Receptor Negative Human Primary Breast Cancer Cells

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Purpose: Previous reports pronounced that human breast carcinomas have a low tumor take rate in nude mice. However, ER-positive cells (e.g. MCF-7), growing in the mammary fat pad (m.f.p.) of female nude mice supplemented with estrogen, can metastasize to the lungs and lymph nodes. To compare the in vivo tumorigenic potential between orthotopic transplantation and heterotopic transplantation of ER-negative human primary breast cancer cells, tumor growth of suspended cells in the m.f.p. (orthotopic) and in the dorsal subcutaneous (s.c.) layer (heterotopic) were examined in female nude mice.

Methods: We have obtained ER-negative primary cells from human breast cancer tissue using the suspension method. These cells were injected subcutaneously into the lumbar region (2×10^6 or 1×10^7 cells/site) and the inguinal mammary gland mammary fat pad (2×10^6 cells/site) of 6~8week-old female nude mice. Mice were divided into two groups consisting of 10 mice each.

Results: The injection of 2×10^6 viable of primary suspension cells gave a 100% tumor take rate in the m.f.p., whereas the same number of cells did not form tumor in s.c. region in 3 months. In addition, 1×10^7 viable cells injected in s.c. region produced tumors in 20% of the mice. However, we can't detect metastasis to the other sites yet.

Conclusion: Our results indicate that the ER-negative suspension cells injected in the m.f.p. of nude mice could be a valuable tool to measure the tumorigenicity. These findings might suggest that interaction between mammary gland stroma to tumor xenograft is needed for efficient growth of ectopic tumor cells in the nude mice.

Curcumin Induces Non-Apoptotic and Non-Autophagic Cell Death Selectively in Highly Invasive Breast Cancer Cells

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Purpose: In this study, we examined the anti-cancer effect of curcumin, a polyphenolic compound from the rhizome of *Curcuma longa*, using various human breast cancer cells.

Methods: We compared the cytotoxic effect of curcumin in mammary epithelial cells and various human breast cancer cells differing in invasiveness. The mode of curcumin-induced cell death in malignant cancer cells was examined using various methods to detect apoptosis and autophagy.

Results: Treatment with curcumin preferentially cytotoxic to highly invasive breast cancer cells such as MDA-MB 231 and MDA-MB 435S cells over weakly invasive T-47D and MCF-7 cells. In contrast, normal breast MCF-10A and human mammary epithelial cells were very resistant to curcumin treatment. Curcumin-induced cell death in malignant cancer cells was non-apoptotic and non-autophagic. We provide evidences that curcumin-induced increase of Ca^{2+} in mitochondria may contribute to severe swelling of mitochondria and ER, leading to irreversible cell death.

Conclusion: Treatment with curcumin may be a safe and effective strategy for treating malignant breast cancer cells.

Expression of HER-2/neu and Paxillin in Ductal Carcinoma In Situ and Invasive Ductal Carcinoma with Ductal Carcinoma In Situ

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Purpose: The mutual operation of protein substances inside and outside cells causes the cells to grow, move, proliferate, differentiate and die. C-erbB2 protein stimulates the genes (HER-2/neu) which produce the epidermal growth factor receptor (EGFR) to distribute more receptors on the cell membrane. Paxillin is a focal adhesion-associated adaptor protein and is known to play a pivotal role in the proliferation or activation of cells.

Methods: To observe the expression of HER-2/neu and Paxillin in 25 cases of ductal carcinoma in situ and 25 cases of invasive ductal carcinoma with ductal carcinoma in situ, the authors performed immunohistochemical staining.

Results: The DCIS was frequently associated with the infiltration of the inflammatory cells, especially in the comedo and solid types. The grade of HER-2/neu in the adjoining normal ductal epithelial cells was low, compared to that of the tumor cells. But, the grade of paxillin in adjoining normal ductal epithelial cells was similar to tumor cells. The expression patterns of HER-2/neu and paxillin in mucinous carcinoma are negative in all cases, which showed that this carcinoma grow slowly.

Conclusion: The expression difference of HER-2/neu between DCIS in IDC and pure DCIS suggested that the place of origin of tumor cells appeared to be different. The paxillin appeared to have no value as a prognostic factor.

siRNA Mediated Downregulation of Estrogen Receptor in Human Breast Cancer Cells

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Purpose: To establish model of breast cancer cell lines with down-regulated estrogen receptor (ER) to simulate loss of ER function, which regulates growth pathways in breast cancer patients that become unresponsive to endocrine manipulation.

Methods: Using liposome-mediated delivery, MCF7 breast cancer cells were transfected with ER siRNA cloned into plasmid vectors containing either constitutive or inducible promoters. Transfectants were selected and expanded. Subsequently, cloned lines were analyzed for the presence of ER mRNA by real-time PCR and for ER protein by western blotting. For lines containing inducible plasmids measurements were made after 24-48 h treatment of cells with 3-5 µg/mL tetracycline. Growth curves were generated over 4 days to determine the responsiveness of transfected cells to estradiol, compared to parental wild type MCF7 cells.

Results: Several stably expressing transformants, which exhibited a reduced amount of ER, were established in long term culture. One line designated pII was further studied in relation to its hormone sensitivity; this showed no growth stimulation by estradiol, in contrast to parental MCF7 cells. Two other lines (E1 and E2) established using the inducible ER siRNA vector also showed reduced amounts of ER when exposed to tetracycline. This agent also showed a growth inhibitory effect which is interpreted as being due to the induced reduction in ER.

Conclusion: Breast cancer cell lines that are refractory to estradiol stimulation have been established in long term culture to provide a model system in which to study the factors that control cell growth in cells that have acquired endocrine resistance. (Supported by Kuwait University Grants PC02/04 and YS01/04).

Characteristics and Prognostic Factors in the Triple-Negative Breast Cancer

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Purpose: Triple-negative breast cancer (estrogen receptor-negative, progesterone receptor-negative, and HER2-negative) is a relatively high risk tumor that lacks the benefit of specific therapy that targets these proteins.

Methods: We reviewed the medical records and pathologic slides of specimen of 913 patients who received curative operation for breast cancer between 2000 Apr. and 2002 Dec. with long-term follow-up (median 50.3 months). We evaluated on the several clinical and prognostic factors, survivals and disease free intervals between triple-negative patients and others.

Results: Most of patients are invasive ductal carcinoma (81.5%). 270 patients (29.6%) who were defined as triple-negative breast cancer (TNBC) compared with 593 patients of non triple-negative breast cancer (NTNBC). TNBC shows larger size of tumor, high expression of p53, many breast cancer-related death and local recurrence than NTNBC. Nuclear and histologic grade is high in TNBC. Overall survival of TNBC is shorter than NTNBC, but disease-free interval is not. In the advanced stage (II/III), breast cancer-related death was higher in TNBC, thus overall survival is poor than NTNBC. But in the early stage disease (stage I), there are no difference between two groups. In TNBC, overall survival is related with the tumor size, lymph node status, lymphovascular (LV) invasion and disease-free interval with LN status, multicentricity, and LV invasion. There is no correlation with the adjuvant chemotherapy. In multivariate analysis of prognostic factors, LV invasion were the most important prognostic factor.

Conclusion: TNBC was related with poor prognostic factors such as larger tumor size, higher expression of p53, high nuclear/histologic grade, high mortality and local recurrence, thus their survival is poorer than NTNBC. Also we concluded that LV invasion is the most significant prognostic factor in TNBC.

Clinicopathologic Characteristics of Invasive Micropapillary Carcinoma of Breast

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Purpose: Invasive micropapillary carcinoma (IMPC) of breast is unusual form of breast cancer characterized by clusters of cells in micropapillary or tubular-alveolar arrangement with in clear spaces. In recent studies, IMPC was associated with the high rate of vascular invasion and axillary lymph node metastasis and poor prognosis. The aim of this study is to reveal distinctive clinicopathologic features of IMPC, compared with invasive ductal carcinoma (IDC).

Methods: Forty-two patients diagnosed as IMPC were analyzed. We evaluated their clinicopathologic findings including age, tumor size, lymph node status, nuclear grade and result of immunohistochemistry and compared these with those of 1,814 patients diagnosed as IDC.

Results: The mean age was 46 years, and mean tumor size was 2.6 cm. There was no significant difference in results of mean age, tumor size, and nuclear grade between IMPC and IDC. In IMPC, the incidence of axillary lymph node metastasis was significantly higher (76.2% vs. 45.1%, $p < 0.001$), especially in T1 and T2 tumors. The expression of progesterone receptor was more frequent in IMPC ($p = 0.005$), while the expression of p53 and c-erbB-2 were significantly frequent in IDC ($p < 0.001$). There was no difference in rate of expression of estrogen receptor. During follow up period, recurrence rate and time to recurrence of IMPC and IDC showed no significant differences.

Conclusion: IMPC showed more extensive axillary lymph node metastasis in relatively small size tumors and frequent expression of progesterone receptor than IDC, while the rate of expression of p53 and C-erbB-2 was lower.

The Role of Wnt-1 and PTEN Expression in Human Mammary Carcinogenesis

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Purpose: There is increasing evidence that the mammary stem cell and progenitor cell might contribute to mammary carcinogenesis. These cells are thought to be targets for transformation through all the windows of breast development. This could cause phenotypic heterogeneity as well as prognostic diversity of breast cancer. This study was conducted to demonstrate how abnormal expression of Wnt-1 or PTEN affects on human mammary carcinogenesis.

Methods: In 31 cases of invasive ductal carcinoma not more than 1 cm, we tested the correlation among immunohistochemical expression of lineage-related biomarkers [cytokertin 18 (CK18), cytokeratin 6 (CK6)], stem cell-related proteins [Wnt-1, PTEN], and histopathologic findings [foci of lesion, the association of in situ carcinoma] on consecutive sections obtained from the same paraffin-embedded tissue block.

Results: PTEN expression was associated with positive CK6 expression. All PTEN-positive cancers were over-expressed with Wnt-1, and showed unifocality of lesion. CK18-positive cancer was significantly associated with over-expression of Wnt-1, not with PTEN expression. CK6-positive cancer was also associated with unifocality of lesion. (by 2-tailed Pearson correlation)

Conclusion: The presumption is that aberrant expression of both PTEN and Wnt-1 gives rise to propagating the self-renewal properties of mutated progenitor/stem cells during mammary development with long latency, permitting the mammary gland to keep on branching, making a field of neoplasm, and eventually causing multi-focal/centric lesion. In case that Wnt-1 is affected only, PTEN could suppress development of mutated progenitor/stem cells, arrest branching process, consequently, keep cancer unifocal.

Is the Specific Subtype of Ductal Carcinoma In Situ a Precursor to the Same Subtype of Invasive Ductal Carcinoma?

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Purpose: We conducted serial analysis for both ductal carcinoma in situ (DCIS) and invasive ductal carcinomas. By analyzing both in situ and invasive cancers concurrently, we attempted to discuss the origin of a specific subtype in invasive ductal carcinoma.

Methods: We retrospectively analyzed a total of 2,701 patients (259 of DCIS and 2,442 of invasive ductal carcinomas) who underwent surgery at our institution for the period between January 2000 and December 2006. DCIS and invasive ductal carcinoma were classified into four subtypes according to hormone receptor (HR) and HER2 protein expression status: HR-expressing, HR & HER2-expressing, triple-negative, and HER2-expressing subtypes.

Results: As DCIS progresses to invasive lesion, the positive rate of HR and HER2 protein decreased from 68.7% to 62.0% and from 39.4% to 20.9%, respectively. The prevalence of each subtype in DCIS was as followed: 142 (54.8%) cases of HR-expressing, 36 (13.9%) cases of HR & HER2-expressing, 15 (5.8%) cases of triple-negative, and 66 (25.5%) cases of HER2-expressing subtype. In invasive lesions, subtypes were 1297 (53.1%), 216 (8.8%), 635 (26.0%), and 294 (12.0%) cases, respectively. HER2-expressing and triple-negative subtypes were associated with high nuclear and histologic grades, p53 overexpression, elevated Ki-67 index, and negative bcl-2 ($p < 0.05$).

Conclusion: Analysis of the changes in HR and HER2 expression and the prevalence of each subtype in DCIS and invasive ductal carcinoma revealed that it is more likely that a specific subtype of invasive carcinoma is determined secondarily by phenotypic changes during tumor progression, rather than arising from the same subtype of in situ lesion.

Molecular Biological Differences between Younger and Older Breast Cancer Patients Based on the Status of a Microsatellite Marker

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Purpose: Younger women exhibit more aggressive pathological features of breast cancer than older women, based on previous studies. We wished to evaluate any molecular biological differences in breast cancer between younger and older women by determining the status of a microsatellite marker.

Methods: Microsatellite instability (MSI) and loss of heterozygosity (LOH) were investigated in paired tumour and normal tissue DNA from 32 younger (age less than 40 years old) and 32 older (age more than 50 years old) breast cancer patients with 12 simple repeated primer sets.

Results: MSI was observed at a single locus in 5 (15.6%) of the younger patients. In older patients, MSI was observed at a single locus in 5 (15.6%) and at multiple loci in 1 (3.1%) of the older patients. The greatest frequency of LOH was at loci UT5320 (37.5%), D8S321 (34.4%), D9S242 (31.3%), and D19S394 (31.3%) in younger patients and at loci L17686 (34.4%) and D19S394 (28.1%) in older patients. LOHs at D9S242 and D8S321 were significantly higher in the carcinoma of younger women ($p=0.013$, $p=0.016$, respectively). The LOH status was unrelated to clinical stage, nodal status, tumour size, histological grade or estrogen receptor (ER) status. A LOH at D8S321 was associated with tumor size ($p=0.048$) and a LOH at UT5320 was associated with histological grade ($p=0.012$) and ER status ($p=0.018$).

Conclusion: These results indicate that the pattern of chromosomal alterations are not exactly the same, especially at loci D9S242 and D8S321, in the carcinomas of the two age groups and suggest that the molecular pathogenesis of the carcinomas is not similar.

Detection of Human Papillomavirus DNA by DNA Chip in Breast Carcinomas of Korean Women

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Purpose: The association between human papillomavirus (HPV) and cervical cancer is well documented. However, it remains unclear whether there is also a correlation between HPV infection and human breast cancer. The aim of this study was to investigate the status of HPV DNA in breast carcinoma of Korean women and to examine the possible association between HPV and breast cancer development.

Methods: We examined the HPV DNA of 154 patients including 123 cases of breast carcinoma, 31 cases of intraductal papilloma, and 27 cases of adequate nipple from cancer patients using DNA-chip method.

Results: The HPV DNA was detected in 8 breast carcinomas (6.5%), but in none of the intraductal papillomas. All detected HPV was high-risk groups; the HPV-18 and HPV-70 were found in each two cases and each one cases HPV-16, 31, 56/58 and 59. In one case of nipple, both low-risk (HPV-62) and high-risk (HPV-18) group HPV DNA was obtained. The papillary carcinomas and the invasive ductal carcinomas with adjacent intraductal papillomas showed slightly increased incidence (11% vs. 3-4%), however, there was no significant difference. No correlation between the presence of HPV DNA and specific prognostic predictors for the disease outcome was observed.

Conclusion: Our results suggest that the presence of high-risk group HPV in the breast might be related to breast carcinogenesis, especially papillary phenotype. Further studies are required.

Results of Three Dimensional Conformal Radiation Therapy for Solitary Sternal Relapse of Breast Cancer

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Purpose: To evaluate the response, survival rate after the radiation therapy in patients with a solitary sternal relapse of breast cancer.

Methods: Between May 1996 and June 2005, 17 patients who received salvage radiation therapy for solitary sternal relapse of breast cancer were evaluated. The radiation treatment was designed using a three dimensional conformal radiation therapy and the treatment fields included the gross tumor volume with 2-cm margins. The radiation dose was 35-61.5 Gy (biologic effective dose of 43.7-76.9 Gy 10 using the α/β ratio of 10 Gy) with 1.8-3 Gy as a daily dose. The tumor response was evaluated by the change in maximum tumor size on CT scans 1-3 months after completion of treatment.

Results: An objective tumor response was achieved in all patients with complete response in 5 patients and partial response in 12 patients. The 5-year overall survival rate was 51.9% (median survival time: 27 months), and this was affected by interval from primary surgery of breast cancer to the development of sternal metastasis (disease-free interval): The 5-year overall survival rate was 61.8% for disease-free interval ≥ 12 months and 0.0% for disease-free interval <12 months ($p=0.03$).

Conclusion: Radiation therapy is effective treatment in patients with solitary sternal relapse of breast cancer. Patients with solitary sternal relapse could survive long term, particular with long disease free interval from primary surgery for breast cancer.

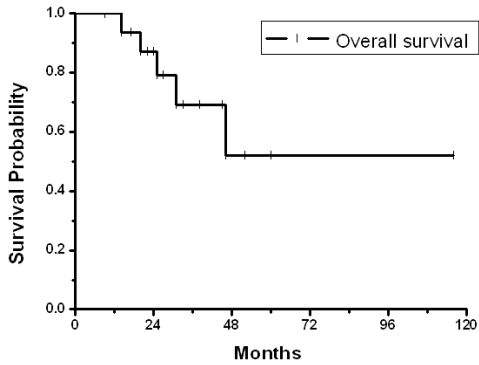


Fig 1. Overall survival

Factor	Number of Patients (%)	3-year Survival rate (%)	p-value [‡]
Age			
≥ 40 years	11 (64.7)	75.0	0.10
< 40 years	6 (35.3)	53.3	
Initial tumor stage*			
I/II	13 (76.5)	65.2	0.80
III	4 (23.5)	100.0	
Systemic therapy followed by sternal radiotherapy			
Yes	9 (52.9)	71.4	0.75
No	8 (47.1)	70.0	
Disease-free interval*			
≥ 12 months	14 (82.4)	82.5	0.03
< 12 months	3 (17.6)	0.0	
Radiation dose (BED[‡] Gy₁₀)			
≥ 65	7 (41.2)	68.5	0.78
< 65	10 (58.8)	76.9	

Fig 2. Univariate analysis

Volume Replacement of Reconstruction Methods for Breast Conserving Therapy by Video-Assisted Breast Surgery

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Purpose: Video-assisted breast surgery (VABS) is a noble surgical method in esthetics and radical treatment of breast cancer. We have performed VABS on 200 patients since December, 2001. We reviewed the reconstruction methods, especially about the volume replacement, for breast conserving therapy by VABS.

Methods: A 2.5-cm axillary and/or periareolar skin incision was made for an approaching port, and a working space was created by retraction. Under video-assistance, we resected the mammary gland partially or totally, and in the case of malignant diseases we also performed a sentinel lymph node biopsy and dissected axillary lymph nodes (levels I and II). The breast reconstruction was performed simultaneously by gland mobilization in 54 patients, by transplantation of lateral chest fat tissue flap (LTF) in 63 patients, and by absorbable fiber mesh or cotton in 83 patients. The aesthetic evaluation was done using our original scoring system, ABNSW, which counts three points for each five items: asymmetry; breast deformity; nipple shape; skin condition; wound scar.

Results: The diseases were benign in 22 patients and malignant in 178 patients. The volume replacement by LTF or absorbable fiber was needed to keep the breast shape in more than 25% partial resection of the breast. The absorbable fiber was useful for replacing the volume defect in thin patients without enough fat tissue around her lateral chest. The esthetic results were good. There was no serious side effect on them.

Conclusion: The volume replacement by absorbable fiber is effective in breast conserving therapy of VABS.

Reexcision or Mastectomy: When Surgical Margin is Involved during Breast Conserving Surgery in Multifocal Invasive Cancers

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Purpose: It is important for breast conserving surgery (BCS) whether a negative surgical margin is obtained or not. However, there is no directional guideline to decide which, reexcision or mastectomy, is desirable when residual cancer remains at surgical margin during the BCS. We sought to analyze the risk factors of margin involvement and the indications for mastectomy.

Methods: A retrospective analysis was conducted for 519 patients with multifocal invasive breast cancers at Asan Medical Center from August 1990 to December 2005.

Results: BCS was initially planned for 132 patients and forty (30.3%) of them had positive surgical margin after the BCS. In addition, the completion mastectomy was performed in 20 patients, so finally 112 underwent BCS. By multivariate analysis, the rate of the positive surgical margin was lower when cancers were located in upper outer quadrant in comparison to the other quadrants (0.33; 95% CI, 0.11 to 0.95). The rate was higher when DCIS coexisted (33.79; 95% CI, 10.87 to 105.05). Nineteen out of forty patients underwent reexcision and twenty underwent completion mastectomy. Conversion to mastectomy was related to multiple margins involvement (6.51; 95% CI, 1.38 to 30.78) and margin involvement of areolar direction (6.29; 95% CI, 1.19 to 33.25).

Conclusion: Special attention is required in BCS for cancers with coexisting DCIS or they are located in quadrant besides upper outer due to high probability of margin involvement. The completion mastectomy is considered when multiple margins or areola direction are involved.

Breast Conserving Treatment for Paget's Disease

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Purpose: Breast conservation for Paget's disease is controversial because it is accompanied with underlying malignancy in majority. Not only removal of nipple-areolar complex but also excision of underlying breast tissue is necessary. The purpose of this study is to demonstrate usefulness of dynamic study of magnetic resonance imaging (dynamic MRI) to determine the indication of breast conservation, and our simple reconstruction method.

Methods: Since 1999, three patients with Paget's disease have been treated with breast conserving treatment in our institute. All of them underwent dynamic MRI to determine the indication of breast conservation. After excision of nipple-areolar complex with underlying breast tissue, the defect was fulfilled with skin flap, medial side was round and lateral V in shape, which was advanced from outside of the defect using V-Y flap procedure.

Results: In all of 3 patients, margin statuses of specimens were negative for cancer and the histological extents of ductal spread well coincided with those diagnosed by dynamic MRI. However, recurrence in the ipsilateral breast occurred in the distant site from the operated wound in one patient who was treated without radiation therapy. Our reconstruction method using V-Y flap could be done without special plastic surgical techniques; moreover, cosmetic outcome was satisfactory.

Conclusion: Breast conserving surgery for Paget's disease can be performed safely according to preoperative dynamic MRI. However, post-operative radiation therapy is necessary. And our simple reconstruction method is satisfactory.

For the Issues of Treatment and Nursing Management, and of Preventive Measures and Diagnostic Process of Breast Cancer

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Purpose: The research will directly to point for the issues of treatment and nursing management, and of preventive measures and diagnostic process of breast cancer.

Methods: The research shall be done using statistics, and quantities and quality analyses, and some dissections came out using stat graphic-5 software.

Results: Throughout the country, between January 2003 to January 2006 or in the last 3 years, 249 persons have got breast cancer disease. And, if we compare the patients by their ages, women in the elderly ages are more reluctant to have taken this breast cancer, and data shows 47.1 persons has got this disease in Mongolian country. If we compare spread level of this disease by the regions, in Selenge, Khovd and Sukhbaatar provinces are higher then comparing to Arkhangai, Uvurkhantai, Bayan-Ulgii and Bayankhongor provinces. Dividing the country in to 3 regions, the east region has 34,42 breast cancer elderly patients in each 100,000 people, the west region has 38 patients, and the central region has 68.91 patients respectively.

Conclusion: 1. We need to establish and develop an evaluation and assessment systems for person's healthiness, and to make and do have constant examinations for breast cancer disease in all over the country. 2. And also, we need to improve quality of treatments for breast cancer, to strengthen preventive measures, and improve capacity level of the professionals especially in the remote areas, and more importantly to develop and strengthen the management systems in breast cancer treatment activities.

Efficacy and Safety of Low Dose Capecitabine in Treatment of Heavily Pretreated Metastatic Breast Cancer Patients with Multiple Liver Metastases

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Purpose: Treatment of the patients with multiple liver metastases has specific therapeutic dilemma. Progress disease cause liver dysfunction that aggravates patient's quality of life, therefore, highly active cytotoxic agent is necessary to improve these situations; however it may cause unpredictable adverse events due to altered liver function. The purpose of this study was to elucidate the efficacy and safety of the low dose capecitabine in treatment of heavily pretreated metastatic breast cancer patients with multiple liver metastases.

Methods: Since July 2003, nine breast cancer patients with multiple liver metastases, pretreated with anthracyclines and/or taxanes, were consecutively treated with oral capecitabine (828 mg/m² twice daily for 3-weeks followed by 1-week rest) in our institute. The efficacy and safety of this regimen were investigated retrospectively.

Results: Of all 9 patients, 7 patients were accompanied with liver dysfunction. Of these 7 patients, 5 patients showed over 2.5 times of upper limits of normal of transaminases. Of the assessable 8 patients, 6 patients had achieved disease control including 2 partial response (PR), 4 stable disease (SD). No grade 3/4 toxicities were observed. 6 patients with disease control had remarkable improvements of liver biochemistry after 2 cycles of capecitabine. The median time to progression and median overall survival were 13.6 and 40.6 weeks respectively.

Conclusion: The low dose of capecitabine was shown to be effective and well tolerated as a salvage treatment for extensive liver metastases of breast cancer.

Curcumin Potentiates the Growth Inhibitory Effect of Paclitaxel through Suppression of Nuclear Factor-kappa B in Breast Cancer

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Purpose: Paclitaxel is an effective anticancer agent for breast cancer, but its major disadvantage is dose-limiting toxicity. Most anticancer agents activate nuclear factor kappa B (NF- κ B), which can mediate cell survival, proliferation, and metastasis. Curcumin has been shown to inhibit the growth of various cancer cells, without toxicity to normal cells. The antitumor effects of curcumin could be due in part to the inactivation of NF- κ B. We hypothesize that blocking NF- κ B activity may augment paclitaxel cancer chemotherapy.

Methods: In this study, we investigated whether the inactivation of NF- κ B by curcumin would enhance the efficacy of paclitaxel for inhibiting breast cancer growth in vitro and in vivo.

Results: We confirmed that curcumin inhibited paclitaxel-induced activation of NF- κ B and potentiated the growth inhibitory effect of paclitaxel in MDA-MB-231 breast cancer cells. The combination of curcumin with paclitaxel elicited significantly greater inhibition of cell growth and more apoptosis, compared with either agent alone. In an experimental breast cancer murine model using MDA-MB-231 cells, combination therapy with paclitaxel and curcumin significantly reduced tumor size and decreased tumor cell proliferation, increased apoptosis and decreased the expression of MMP-9 compared with either agent alone.

Conclusion: These results clearly suggest that a curcumin-paclitaxel combination, which inactivates NF- κ B activity, may contribute to increased cell growth inhibition and apoptosis, thus augmenting paclitaxel chemotherapy, could be a novel strategy for the treatment of breast cancer.

Combinatory Therapy between Tetramethoxystilbene and Growth Factor Signaling Inhibitors in Hormone-Resistant Breast Cancer Cells

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Purpose: Tamoxifen and other aromatase inhibitors have been remarkably successful in the treatment of hormone-dependent breast cancer. In case of recurrent cancer cells, they acquired resistance to anti-hormonal therapy through up-regulation of growth factor signaling pathway. Although there are many efforts to enervate these pathways by partial inhibitors, it is not sufficient to overcome the hormonal therapy resistance in breast cancers. We reported that tetramethoxystilbene (TMS) induced apoptosis by inhibiting tubulin polymerization, FAK, Akt, and mTOR and stimulating JNK and MAPK activity. We examined the combinatory effects of TMS and growth factor signaling inhibitors for MCF7 ER(+) cell lines.

Methods: We tested cell proliferation in parental, tamoxifen-resistant (TamR), long-term estrogen deprived (LTED) and ICI-resistant (ICI-R) MCF7 ER(+) cells by combination of TMS and following inhibitors; PI3Ki, mTORi, MAPKi, AKTi, EGFRi, and IGERi.

Results: TMS reduced cell counts of all tested MCF7 cell lines. In combinatory assay, TMS exhibited combinatory effects with other inhibitors, and TMS in combination with PI3K inhibitor was highly effective for decreasing cell counts. LTED cells were more sensitive to a combination of TMS and E2 as well as TMS and PI3K inhibitor. Furthermore, PARP was degraded by TMS and PI3K inhibitor and treatment with both increased cleavage of PARP while PARP cleavage was blocked in the presence of zVAD.

Conclusion: TMS in combination with other inhibitors inhibited cell proliferation by increased apoptosis in hormone-resistant breast cancer cells. These results lead us to expect that TMS may be an therapeutic agent model to control hormonal resistance of ER(+) breast cancer.

A Case of Breast Cancer Showing Rapid Progression during Preoperative Chemotherapy

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We experienced a case of breast cancer that showed rapid progression after success once during preoperative chemotherapy. A 41 years old woman referred to our institution due to a 4.9 cm sized tumor in upper lateral segment of the right breast with 2.3 cm sized palpable axillary lymph node. (T2, N1, M0, stage IIB.) Core needle biopsy and subsequent immunohistochemical examination of the specimens were performed. It was diagnosed as invasive ductal carcinoma, ER+, PgR±, Her2-. Neoadjuvant chemotherapy with 6 courses of FEC100 followed by 12 courses of weekly paclitaxel (80 mg/m²) was scheduled. The breast tumor was decreased to 3.6 cm in the maximal diameter, and the swollen axillary lymph node became to 1.0 cm after 6 courses of FEC, estimated partial sponse. Despite of the good response, the tumor grew up to 5.1 cm after six courses of weekly paclitaxel. Though 2 courses of FEC were administered again, the tumor progressed rapidly becoming to 17 cm in diameter. A mastectomy was performed to control high fever, pain and anemia due to the huge tumor. A pathological examination revealed invasive ductal carcinoma (solid-tubular type), ER-, PgR-, Her2-. Interestingly endocrine responsiveness of the tumor was differed from the biopsy specimen obtained before chemotherapy. It is necessary to accumulate these cases because there is no liable evidence or direction against rapid disease progression during primary chemotherapy.

Incidence of Chemotherapy-induced Amenorrhea in Young Patients with Breast Cancer after Adjuvant Chemotherapy

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Purpose: Premenopausal women are about 60% of all breast cancer patients in Korea. Although chemotherapy can improve the survival rate of these patients, it also could induce the premature menopause. The objective of this study was to determine the incidence of amenorrhea in women with breast cancer age 45 years and younger after adjuvant chemotherapy.

Methods: Patients who have invasive breast carcinoma treated with adjuvant chemotherapy from January 2003 to December 2005 were included. Amenorrhea was defined as the absence of menstruation for 3 months in succession or serum follicular stimulating hormone level >40 mIU/mL after the completion of all chemotherapy. All patients were premenopausal.

Results: Total 162 patients were included. The median age of patient at diagnosis was 41 years (range, 26-45 years). The chemotherapy regimens were CMF (n=121), AC (n=14), FAC (n=4), doxorubicin plus taxotere (n=6) and AC sequenced by taxane (n=17). 131 patients (80.9%) developed amenorrhea. The expected amenorrhea rate at 6 months, 12 months and 24 months after chemotherapy were 74.7%, 69.1%, and 60.75%. Women who experienced amenorrhea were found to be significantly older than women who did not (p=0.000). Thirty-eight patients (29.0%) resumed menstruation. Women who recovered from amenorrhea were significantly younger than women who did not (p=0.000). Patients treated by CMF were poorly recovered from amenorrhea (p=0.000).

Conclusion: Age of patient is most important factor for inducing amenorrhea after chemotherapy. Patient with older age or CMF chemotherapy regimen has difficulty in recovering from chemotherapy-induced amenorrhea. To increase the information available to assist young patients who are considering adjuvant therapy, prospective studies should be performed.

Toxicity and Impact of Prophylactic G-CSF in Korean Breast Cancer Patients Receiving Adjuvant TAC Regimen Chemotherapy

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Purpose: More recently, BCIRG 001 has shown that the TAC regimen is superior to FAC as adjuvant chemotherapy for node-positive operable breast cancer. Unfortunately, TAC was clearly more toxic than FAC, not only with respect to neutropenic fever events, but also with respect to many extra-haematological side-effects. The purposes of this study were to analyse the toxicity and tolerability of Korean breast cancer patients treated with TAC, to evaluate impact of adding secondary prophylactic G-CSF to the TAC regimen.

Methods: This study was carried out in 50 axillary node positive breast cancer patients who underwent primary surgery at the Department of Surgery in Soonchunhyang University (4 affiliated hospitals) from October of 2005 to March of 2007. They received a total of 260 courses consisting of TAC (75/50/500 mg/m² 6xq3wk). Toxicity was graded according to the NCI CTC version 2.0.

Results: The main toxicities were hematologic (neutropenia grade 3/4 in 100% of patients and 95.6% of cycles; febrile neutropenia in 38% of patients and 15.9% of cycles). There was no cases of septic death. The peak time of occurrence of febrile neutropenia was 7-10 days after receiving chemotherapy. Severe non-hematologic adverse events were infrequent; myalgia (30%), fatigue (22%), stomatitis (20%). The TAC with prophylactic G-CSF regimen yielded a statistically reduction in the incidence of nausea ($p=0.01$), stomatitis ($p=0.032$), myalgia ($p<0.001$) and the duration of febrile neutropenia ($p=0.024$).

Conclusion: Adjuvant chemotherapy with TAC was tolerable in Korean breast cancer patients. Although neutropenia is frequent, its consequences are manageable. The addition of prophylactic G-CSF reduce that of some TAC-induced hematological and extra-hematological side effects.

Rehabilitation of Breast Cancer Patient: Review of the Literature and Services of Hospitals Words

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Purpose: The aim of study was to suggest the rehabilitation model of Breast Cancer Patient through the review of the literature and the hospitals services related to rehabilitation of breast cancer patients.

Methods: A literature search covering was carried out using five electronic databases; medline, Cinahl, PsycLit, and Academic Search databases. The key-words used in search were rehabilitation, breast, cancer. The search strategy used both the index systems and the free-text searching. The review of hospital services for breast cancer patients in general hospitals were done through internet search. To suggest the model for rehabilitation of breast cancer patients were done through the thematic content analysis to achieve the main concepts and the meaning of those concepts about breast cancer rehabilitation in literature review about rehabilitation of breast cancer patients and the hospital services for breast cancer patients.

Results: Rehabilitation of breast cancer patients were related to physical and cosmetic, psycho-social, cognitive behavioral, informational and symptom management. 1) Physical and cosmetic rehabilitation: physical activity, exercise (multi joint exercise etc.), shoulder range of movement, tailored exercise. 2) Psycho-social rehabilitation: peer support, group support, complementary therapy, icsussion of psycho-social issues. 3) Cognitive behavioral rehabilitation: relaxation, distraction, massage, recreation, stress management, techniques for handling anxiety, problem solving, discovering, challenging automatic negative thoughts. 4) Informational rehabilitation education about predisposing factor, diagnosis, treatment of breast cancer, diet, reconstruction of breast, side effects of treatment. 5) Symptom management: pain, lymphedema, body weight control.

Conclusion: Effective rehabilitation should be considered the physical, emotional, social, and economical status of breast cancer patients.

Close or Positive Margins Following Mastectomy for Pure DCIS: Recurrence Rates and Potential Indications for Radiotherapy

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Purpose: Mastectomies generally result in very high local control rates for pure DCIS. However, close or involved tumor margins are occasionally encountered despite this radical procedure. Data regarding recurrence rates in this setting is virtually non-existent. This review represents our institution's experience with these patients.

Methods: From 1994-2002, the pathology reports of 574 patients who underwent mastectomies at our institution for pure DCIS were retrospectively reviewed. Eighty non-irradiated patients were found to have margin of less than 10 mm. Thirty-one patients had <2 mm margins whereas 49 patients had margins of 2.1-10 mm. High grade disease was observed in 47 patients. Forty-five patients had comedonecrosis. Fifty one patients were under 60 years of age. Thirty patients had multifocal disease.

Results: With a median follow up of 61 months, 6 of 80 (7.5%) patients had local recurrences. Chest wall recurrences were noted in five patients with one patient having a recurrence in the axillary tail. Five out of the 31 patients (16%) with a margin of 2 mm or less locally recurred versus only one out 49 (2%) for patients with margins of 2.1-10 mm ($p=0.03$). No patients with low grade disease or over the age of 60 had a local recurrence regardless of margin status.

Conclusion: This review suggests that patients with pure DCIS who have undergone mastectomies with margin <2 mm have a higher-than-usual incidence of local recurrence, particularly if they have additional unfavorable features such as high grade disease or age <60. These patients may benefit from chest-wall radiotherapy.

Predictors of Mastectomy in a Certified Breast Center – The Surgeon is an Independent Risk Factor

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Purpose: The current study examined predictors of mastectomy in a certified breast center with the main impact on the factor surgeon.

Methods: 663 patients were analyzed for their mastectomy rates. Included were patients with T1 and T2 tumors, who had their surgery performed by one of three specialized breast surgeons with a workload of at least 50 new breast cancer cases per year.

Results: On multivariate analysis central tumor localization, positive lymph node status, non-unifocality, large tumor size and the surgeon were independent predictors of mastectomy. Surgeon A had a mastectomy rate of 30.5% (50/164), surgeon B 26.9% (43/160) respectively and surgeon C had a mastectomy rate of 15.8% (27/171), $p=0.005$. Patients, who had surgery performed by surgeon A or surgeon B were 2.34 (95% CI 1.38-3.97, $p<0.005$) respectively 1.96 (95% CI 1.14-3.36, $p=0.01$) times as likely to have a mastectomy than patients who had surgery performed by surgeon C.

Conclusion: Even in a certified breast center with specialized breast surgeons the surgeon is an independent risk factor of mastectomy, as the tumor criteria are given at the time of diagnosis.

A Quilting Effect on Seroma Prevention of Latissimus Dorsi Myocutaneous Flap (LDMF) Donor Site

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Purpose: Seroma is the most common complication in latissimus dorsi muscle flap donor site, despite the use of closed suction drains. Problems of seroma are patient's discomfort, repeated aspiration, wound infection, dehiscence and flap necrosis. Therefore prevention of seroma on donor site can help healing course of breast conserving surgery (BCS). The aims of present study were evaluated the quilting effect of seroma prevention and the efficacy of quilting technique.

Methods: Ninety-five patients who had diagnosed invasive ductal carcinoma received immediate LDMF reconstruction after BCS, from Mar. 2006 to Feb. 2007. They were divided two groups; Group A (44 cases) was LDMF with quilting and closed suction drain, Group B (51 cases) LDMF with only closed suction drain. Outcome measures age, BMI, mastectomy volume, total drain, drain removal day, in-hospital stay and presence of aspiration.

Results: The mean age of patients (43.8 vs. 45.3), BMI (22.5 vs. 22.3), mastectomy volume (290.7 vs. 334.1) were statistically insignificant. Quilting reduced overall seroma volume (725.0 vs. 1138.1, $p=0.0004$), drain removal day (8.2 vs. 10.6, $p<0.0001$), and in-hospital stay (11.5 vs. 14.3, $p=0.002$). Aspiration of out-patient was done 4 cases of group A and 12 cases of group B ($p=0.06$).

Conclusion: Quilting significantly reduced postoperative seroma volume and in-hospital stay. Seroma incidence in out-patient may be lowered if more data are collected. Quilting is easy, simple technique, and effective method for controlling the seroma formation after LDMF.

Immediate Conservative Breast Reconstruction Technique Using Lateral Thoracodorsal Fasciocutaneous Flap (LTFF)

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Purpose: A lateral thoracodorsal fasciocutaneous flap (LTFF) is a local fasciocutaneous flap that has been used in breast reconstructions since the 1980s. Although the LTFF is a well-studied reconstruction procedure after radical surgery in Western countries, there is no report in Korea. By means of introducing the LTFF procedure, we intend to suggest an easy reconstruction technique that can be performed by the breast surgeon directly.

Methods: Patients with lateral breast cancer and redundant lateral thoracic region might be candidates for this procedure. The flap consists of the lateral and dorsal extensions of the inframammary fold as well as an extended line from the anterior axillary line. A quadrantectomy is performed through a planned skin incision, and an axillary lymph node dissection can be performed simultaneously if the sentinel lymph node is positive. The skin and subcutaneous fat with the fascia of the serratus anterior and latissimus dorsi muscle should be dissected carefully. A wedge-shaped flap can be acquired successfully. The lateral breast defect is then reconstructed by a rotation of the flap. The axis of the flap is drawn following the inframammary fold so that the final scar would be under the brassiere line.

Results: Five patients were treated with the LTFF after breast conserving surgery. All tumors were located in lateral breast regions. The cosmetic result based on four-point scoring system of breast cosmesis showed excellent in four and good in one.

Conclusion: With appropriate patient selection, LTFF might be a useful method for breast reconstructions.

Mammotome Biopsy with Mammography Guided Wire Localization for Clustered Microcalcifications

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Purpose: The pre-operative diagnosis of clustered microcalcifications usually requires stereotactic mammotome biopsy. The aim of this study was to evaluate whether mammotome biopsy following digital mammography guided wire localization for clustered microcalcifications without associated sonographic or palpable masses was useful.

Methods: Fifty consecutive patients who have clustered microcalcifications on screening mammography underwent mammotome biopsy. The lesion itself is not seen on ultrasound imaging. To find the accurate location of clustered microcalcifications, fix the wire and sheath on breast parenchyma. And then during mobilizing the sheath, the ultrasound is revealed wire-inserted site in clustered microcalcifications. Then ultrasound-guided mammotome probe is inserted in the lower parts of sheath as possible as parallelly. Mammotome biopsy carry out tissue sampling for 3-4 times to make hematoma. Then we can predict the lesion following by removal site of wire and sheath where remained hematoma. By the way of specimen mammography, we can verify that mammotome biopsy has been successful.

Results: Microcalcifications were visible on specimen mammography and microscopic slides in forty-eight (96%) patients. Forty-two (84%) of benign, five (10%) of ductal carcinoma in situ, two (4%) of invasive ductal carcinoma, one (2%) of invasive lobular carcinoma were diagnosed on biopsy. Except benign cases, eight patients underwent breast conserving surgery.

Conclusion: The mammotome biopsy with ultrasound after distal mammography guided wire localization may be useful in the detection and successful biopsy of clustered microcalcifications without associated sonographic or palpable masses.

Long Term Follow up Results of Nipple Areola Skin Sparing Mastectomy in Breast Cancer

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Purpose: Nipple-areolar preservation is a logical step in the ever more conservative management of breast cancer. Few investigators have reported their long-term experience with procedures that spare the nipple areola complex (NAC). We report here the long term follow-up result of nipple-areola-skin sparing mastectomy (NASSM).

Methods: From 1996 to 2005, 176 patients underwent SSM (54 mastectomies) or NASSM (124 mastectomies), with 2 patients undergoing bilateral operation, yielding a total of 178 mastectomies. No patients received radiotherapy. During performing NASSM, frozen section analysis of the tissue beneath NAC was performed. After the procedure, all patients were followed-up for evidence of recurrence.

Results: The mean age of patients was 39.8 years (ranges, 20-59 years). NAC base was positive in 29.2% patients at definitive histology with false-negative results in 1.6% patients at intraoperative frozen section. Neoplastic NAC involvement was more common in tumor with invasive histology ($p=0.024$) and with extensive intraductal component ($p=0.025$). Other primary tumor characteristics, including multicentricity and location, were not predictive for neoplastic NAC invasion. During the mean follow-up of 56 months, 10 (8.1%) of 124 NASSM patients and 4 (7.4%) of 54 SSM patients developed local recurrences (LR) ($p>0.5$). Local recurrence free interval was not different between the two groups ($p>0.5$). All LRs were detected easily, by patient or routine follow-up check of 6-month interval, and manageable surgically. One patient in SSM group developed distant metastasis at 24 months after the treatment of LR.

Conclusion: NASSM can be a reasonable option for selected patients who want immediate breast reconstruction.

Mammotome Excision for Benign Breast Disease – 3,009 Cases Experience in Single Institute by One Surgeon

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Purpose: The mammotome (MMT) breast biopsy is a new surgical technique that is a minimally invasive, image guided procedure. With the advancement of the techniques of MMT instruments and techniques, there have been many trials to remove the benign lesions with the curative intention. The aim of this study was to evaluate the efficacy and the safety of the MMT biopsy device for percutaneous removal of breast masses.

Methods: From Jan. 2003 to July. 2007, a total of 3,009 US-guided excisional MMT biopsies were performed in 2,419 patients at Kangnam Cha Hospital. Those lesions with BI-RADS category 3 and 4a features by USG examination were included in this study. USG follow-ups were performed 3-6 months later to assess the residual tissue and scarring.

Results: The mean patient age was 36.8 (range: 13-76) years. The average size of lesion was 1.10. Among the patients, 60.2% had nonpalpable lesion and 39.8% had palpable tumor. Most of specimens (70.6%) consisted of fibroadenoma and fibrocystic changes. 48.9% (1,471 lesions) had fibroadenoma, 15.4% (464 lesions) had fibrocystic changes, 2.7% (80 lesions) had intraductal papilloma and 78 lesions (2.6%) were malignant. The mean MMT procedure time was 4.7±3.2 minutes and the mean number of cores removed was 12.5±8.5. No serious bleeding or infection occurred postoperatively.

Conclusion: The present study demonstrates that 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.

Is Surgical Excision Necessary for Benign Phyllodes Tumor of the Breast Diagnosed and Excised by Mammotome Device

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Purpose: Phyllodes tumors are characterized by a double layered epithelial component arranged in cleftlike ducts surrounded by a hypercellular spindle-celled stroma. Recently percutaneous removal of benign breast tumor by Mammotome has been regarded as a feasible, safe method without serious complications. The aim of this study was to evaluate the efficacy and the safety of Mammotome biopsy device in the treatment of benign phyllodes tumor and to identify if surgical excision is necessary for benign phyllodes tumor diagnosed and excised by Mammotome.

Methods: From Jan. 2003 to Feb. 2007, a total of 2,751 US-guided mammotome excision were performed in 2,226 patients at Kangnam Cha hospital. Out of 2,751 lesions, 30 lesions were proved to be benign phyllodes tumor. All lesions were removed by 8 gauge probe. Ultrasonographic follow-up were performed on 3-6 months interval. Mean follow up period were 33.2 months.

Results: Mean patient age was 31.4 years. The average size of lesion was 1.5 ± 0.43 cm. The majority of lesions, 73.3% (22 cases), were palpable and 26.7% (8 cases) were nonpalpable. 22 lesions (73.8%) were classified as BIRADS category 3, 8 lesions (26.7%) were classified as category 4A by ultrasound. During follow up period local recurrence developed in only 1 patient, local recurrence rate was 3.3%. And there were no distant metastasis.

Conclusion: Benign phyllodes tumor found on mammotome excision may not need surgical reexcision if surgeons are sure that the targeted lesions were excised completely and the follow up ultrasound does not show any residual lesions, especially in small phyllodes tumors.

The Scoring System to Predict Non-SLN Status in Breast Cancer Patients with Metastatic SLN: Comparison with Other Prediction Model

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Purpose: About half of breast cancer patients are free from ALN metastasis. Also more than half the breast cancer patients with metastatic-SLNs do not harbor additional metastasis in NSLNs. But it is unclear which patients with metastatic SLNs require a cALND. The aim of this study is to evaluate predictive factors of NSLN involvement in patients with metastatic-SLN, in order to develop a scoring system for predicting NSLN metastasis.

Methods: We reviewed the medical record of invasive breast cancer patients who underwent SLNB at our institution between Jan. 2004 and Dec. 2006. Univariate and multivariate analysis was used to develop a new scoring system for prediction of NSLN status in breast cancer patient with metastatic SLNs. ROC curves were drawn and the areas under the curves were calculated to assess the discriminative power of our and other scoring systems.

Results: A total of 214 patients had a positive SLN and underwent cALND. Multivariate analysis revealed that ALN status in USG ($p=0.0004$), LVI ($p=0.01$), pathologic tumor size ($p=0.04$), numbers of metastatic SLNs ($p=0.006$), and proportion of positive SLNs ($p=0.007$) were independent predictors of metastatic NSLN. The areas under the ROC curves were 0.822, 0.661 (M.D. Anderson), 0.736 (Louisville Breast SLN study), 0.706 (Tenon Hospital), and 0.765 (MSKCC-Nomogram).

Conclusion: The likelihood of metastatic NSLN correlated with ALN status in USG, increasing size of primary tumor, presence of LVI, and increasing number and proportion of metastatic SLNs. A scoring system, consisted with correlated factors may help which patients would benefit from cALND.

Early Result: Volume Replacement with Polyglatin910 Mesh for Breast Reconstruction after Endoscopic Breast Conservative Surgery of Early Breast Cancer

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Purpose: We introduce a new technique with Vicryl mesh made by Polyglatin910 for breast reconstruction after breast conserving surgery.

Methods: Nine patients who underwent endoscopic breast conserving surgery and reconstruction (volume replacement with Vicryl mesh) were evaluated for quality of life (QOL), surgery related complications and cosmetic outcomes. Four patients were excluded; two were lost to follow-up, one required mesh removal due to infection and the other had a total mastectomy due to resection margin positive disease.

Results: The patient ages ranged from 41 to 61 (mean: 45); they all had an early breast cancer diagnosis (less than stage 2b). In general, the patients were satisfied with the outcome with regard to their quality of life. They were especially satisfied with the cosmetic outcome. The satisfaction increased with longer followed up compared to shorter intervals. At 10 months after surgery, the skin and breast shape recovered, and there was encapsulated granulation tissue within tissue fluid collection on ultrasonography.

Conclusion: The results of this study showed that with a relatively short follow up breast reconstruction with Polyglatin910 mesh and oxidized regenerated cellulose, resulted in satisfactory cosmetic results and quality of life after breast conservative surgery.



Fig 1. Postoperative image

Predictive Factors of Nipple Areolar Complex Invasion in Breast Cancer Patients with Mastectomy

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Purpose: Skin-sparing mastectomy with nipple areolar complex (NAC) preservation improves aesthetic outcome for breast cancer patients. This study was performed to investigate predictive factors of NAC-base neoplastic involvement to define the indications for NAC preservation.

Methods: A retrospective analysis of 198 mastectomy patients was conducted to determine the frequency of malignant NAC invasion. The association between NAC involvement and predictive factors, including tumor size, axillary nodal status, nuclear grade, hormone receptor status, tumor multiplicity, tumor location, tumor nipple distance (TND), and lymphovascular invasion (LVI), was evaluated.

Results: The overall frequency of malignant nipple involvement was 19 of 198 (9.6%). Significant differences were found in tumor size, axillary nodal status, tumor nipple distance, TND, and LVI. According to this study, clinical contraindications for NAC preservation include tumors >2.4 cm, positive axillary lymph node, TND <4 cm, and positive LVI.

Conclusion: NAC preservation can be possible in selected patients if we consider the possibility of pre or intraoperative measurement, tumor size, axillary nodal status, TND, and LVI evaluation.

The Axillary Arch of Langer (Axillopectoral Muscle) – Muscular Variation in the Axillae

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Purpose: We report a case of breast cancer patient who had a ‘The axillary arch of Langer’ — the most common anatomical variant of the axillary musculature.

Methods: Patient is a 33-year-old woman who visited the breast clinic due to a 6 cm sized mass on her right breast, which was diagnosed as breast cancer. She underwent modified radical mastectomy and was identified an abnormal muscle originated from latissimus dorsi and inserted to trilaminar tendon of pectoralis major.

Results: During axillary dissection, the muscle interfered level I area due to its longitudinally oblique direction. We separated this muscle, and dissected medial axillary group and lateral axillary group carefully. After 2 years follow up, she has no symptom of recurrence, lymphedema and limitation of motion.

Conclusion: The axillary arch of Langer was first confirmed by Langer in 1864. The incidence is about 7% or less of the population. Despite the reported frequency, its presence is rarely reported clinically. The danger to a breast surgeon of not recognizing an axillary arch muscle abnormality is that dissection along the lateral edge, as if it were the true Latissimus Dorsi, leads superior and anterior to the axillary vein. Any disruption to the lymphatic trunks of the upper limb or injury to the brachial plexus is likely to occur above the axillary vein and a full clearance of the Level I lymph nodes may not be achieved.



Fig 1. The forceps indicated ‘the axillary arch of Langer’

Cryotherapy of Breast Cancer under Ultrasound Guidance: Initial Results and Limitations

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Purpose: The aim of this study was to investigate the potential and feasibility of ultrasound-guided cryotherapy in breast cancer.

Methods: Institutional review board approval and patient consent were obtained. Ten female patients with 10 breast cancers were treated. A 3-mm cryo probe was placed in the tumour under ultrasound guidance. Two freeze/thaw cycles with durations of 7-10 min and 5 min, respectively, were performed. The size of the iceballs were measured sonographically in 1-min intervals. The patients underwent surgery within 5 hours and the specimens were evaluated histologically.

Results: The mean diameter of the iceball was 25 mm after the second freezing cycle. No severe side effects were observed. Three tumours with a diameter below 15 mm did not show and remaining invasive cancer after treatment. In 7 patents cryotherapy of tumours reaching diameters of 25 mm or more resulted in incomplete necrosis.

Conclusion: In tumours larger than 15 mm two of more cyro probes should be used to achieve larger iceballs.

Axillary Recurrence of Breast Cancer after Negative Sentinel Lymph Node Biopsy

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Purpose: Sentinel lymph node biopsy (SLNB) is gaining popularity over axillary lymph node dissection for the detection of node-negative breast cancer, as it is less invasive and false negative results are generally less than 22%. However, regional node recurrence is a major concern for those whose cancer is detected by SLNB. We conducted a retrospective analysis of patient outcomes for those who had received SLNB to assess the rate of recurrence.

Methods: We examined the charts of 720 patients who had been diagnosed with breast cancer between December 2003 and January 2006 and whose SLNB was negative. Of this sample, 174 patients underwent the SLNB and axillary dissection; 453 patients had an SLNB and node sampling; 93 received only the SLNB. The SLNB was performed using a 99mTc-radiocolloid subareolar injection.

Results: The mean number of sentinel lymph nodes removed was 2.1 per patient. At a median follow up of 26 months (range 16-48 months), recurrence appeared in only 3 cases. All three had originally received only the SLNB; all three were also hormone receptor negative. Two of the cases were also c-erbB2 negative. All three recurrences occurred in the axilla; in two of the cases, there was also a recurrence in the internal mammary lymph node.

Conclusion: Axillary recurrence of breast cancer is low in patients who receive an SLNB. For those who are also hormone receptor negative, however, it may be important to also sample lymph nodes and examine internal mammary lymph nodes.

Can Methylene Blue Only be Useful in Sentinel Node Biopsy for Breast Cancer?

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Purpose: Several major institutes in Korea now decide whether to perform a complete axillary dissection based on the sentinel node (SN) status. However, there still have been several limitations in using the isotope or isosulfan blue in Korea. This study was conducted to explore the values of methylene blue (MB) as a mapping dye of SNB in breast cancer.

Methods: From February 2006 to April 2007, 68 SNBs were performed with using MB by subareolar injections in breast cancer patients with clinically negative axilla. A completion axillary dissection was performed in all patients who failed to identify SN, in all patients with tumor positive SN or on the validation purpose. SNs were analyzed by frozen section intraoperatively. We analyzed the identification rate and the factors that might impose on its success.

Results: SNs were successfully identified in 63 of 68 cases (92.6%) with using MB only method. There was no reported anaphylactic reaction. High failure rate only associated with prior excisional biopsy ($p=0.02$). No impact of the patient's age, tumor size, medial tumor location, and operation method on identification rate was found. Among 63 cases with success, 12 (19%) harbored metastatic disease and SNs were the only positive LNs in 9. All five who failed to identify SN had no LN metastases. No false negative was found in 11 validation cases.

Conclusion: MB dye can be considered as a safe and useful alternative to isosulfan blue for SNB in early breast cancer patients. The prior excision might preclude the success of SN identification.

Is the Rate of Local Recurrence after Breast Conservation Therapy affected by How Wide the Negative Margin is?

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Purpose: The purpose of this study was to evaluate the local recurrence (LR) rate according to the margin width and clinicopathologic characteristics of primary tumor, and to evaluate that wider negative margin width is obligatory to prevent LR after breast conservation therapy (BCT).

Methods: We performed 348 BCT for T1 and T2 breast cancer from 1997 to 2004. Negative margin was defined as having more than 5 mm margin distance and close margin was defined as having no more than 5 mm margin distance.

Results: During the mean follow up of 37.2 months, 3.7% (13/348) of patients suffered from LRs. LR rates were significantly associated with young patient age (<40 years, $p=0.009$), high nuclear grade ($p=0.032$), large tumor size (>2 cm, 0.021) and negative hormone receptor ($p=0.032$). Positive axillary lymph node, presence of EIC, high histologic tumor grade, high proliferative index (Ki-67), presence of lymphovascular invasion, over-expression of c-erbB2 and expression of p53 did not achieve statistical significance ($p>0.05$). Among 348 patients, 30 (8.6%) had a close margin and the mean margin distance of these patient was 2.3 mm. The LR rates for patient with a close margin and negative margin were 6.7% (2/30) and 3.5% (11/318), respectively ($p>0.05$). LRs of close margin group were observed only in patients with 1 mm margin distance (13.3%, 2/15).

Conclusion: In conclusion, if the margin distance from cancer is more than 1 mm, the tumor-free margin width did not correlate with increased LR rate.

The Analgesic Effects of Intercostal Nerve Block in Patients Undergoing Augmentation Mammoplasty

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Purpose: Augmentation mammoplasty is a procedure that expands the breast tissue and pectoral muscle by insertion of an implant. This procedure induce extreme postoperative pain. The purpose of this study was to determine whether intercostal nerve block (ICNB) could reduce the pain after augmentation mammoplasty.

Methods: Eighty three patients, who underwent augmentation mammoplasty, at the M.D. Clinic between December 2005 and February 2006, were the cases of this study. We injected 0.25% ropivacaine (total 30 mL per side) in the ICNB group (n=68) into the 3rd, 4th, 5th and 6th intercostal spaces following induction of general anesthesia for surgery. The mean arterial pressures and heart rates were measured before and after subpectoral dissection. A numerical rating scale (NRS: 0= no pain, 10= most severe pain) was used to measure the pain postoperative 6, 24, 48 hours, respectively. We statistically compared the ICNB group with the control group (n=15) with using the Mann-Whitney Rank Sum test.

Results: The mean arterial pressures and heart rates were more stable during subpectoral dissection in the ICNB group than in the control group (p=0.142 and p=0.037). The NRSs were lower throughout the 48 hours of the postoperative period in the ICNB group than in the control group (p<0.001 at 6 hr, p=0.017 at 24 hr, p=0.054 at 48 hr).

Conclusion: ICNB induced stable vital sign during subpectoral dissection and excellent postoperative pain control during 48 hours postoperatively for those patients undergoing augmentation mammoplasty. This procedure will be useful to other breast surgery such as total or partial mastectomy.

Radiation-Induced Pulmonary Toxicity Following Adjuvant Radiotherapy for Breast Cancers

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Purpose: We tried to evaluate the incidence and potential predictive factors for symptomatic radiation pneumonitis (SRP) and radiographic pulmonary toxicity (RPT) following adjuvant radiotherapy (RT) for patients with breast cancer focused on the correlation of RPT with dose volume histogram parameters based on the 3-dimensional RT planning data.

Methods: From September 2003 through February 2006, 171 patients with breast cancer were treated with adjuvant RT following breast surgery. Serial follow-up chest radiographs were reviewed by a chest radiologist. RTOG toxicity criteria were used for grading SRP and a modified WHO grading system was used to evaluate RPT. Overall percentage of ipsilateral lung volume and mean lung dose (MLD) were calculated. We divided ipsilateral lung into two territories, and defined separate DVH parameters to assess relationship between these parameters and RPT.

Results: Four patients (2.1%) developed SRP (three grade 3 and one grade 2, respectively). When 137 patients treated with 3D-RTP were evaluated, 13.9% developed RPT in Tangent territory and 49.2% of 59 patients with regional RT developed RPT in SCL territory. Regional RT and age were significantly correlated with RPT. All DVH parameters except V15 TNGT showed significant correlation with RPT ($p < 0.05$); MLD TNGT was better predictor for RPT for TNGT territory than V15 SCL for SCL territory.

Conclusion: The incidence of SRP was acceptable with the RT technique we used. Age and regional RT were significant factors to predict RPT. DVH parameter was good predictor for RPT in SCL territory while MLD TNGT was better predictor for RPT in TNGT territory.

Clinical Experience of Simultaneous Multitarget Irradiation Using Tomotherapy in Pulmonary Metastasis of Breast Cancer

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Purpose: We analyzed the short term results of simultaneous multitarget irradiation using tomotherapy in lung metastasis of breast cancer to know whether it could substitute surgical metastasectomy.

Methods: We treated ten patients using tomotherapy. The average number of pulmonary metastatic nodules was 3.5. The unilateral and bilateral lesions were in four and 6 patients. In 4 patients, synchronous extrapulmonary targets were present. Nine patients had been treated with chemotherapy for pulmonary metastasis before tomotherapy. The median number of cycles of systemic chemotherapy was twelve and the median interval between chemotherapy and tomotherapy was 1.5 months. We immobilized the patients with BodyFix system (Medical Intelligence, Germany) and prescribed 50 Gy with 10 fractionations for 2 weeks to gross tumor volumes by chest CT scan. We checked megavoltage CT scan to confirm the positions of the targets and the isodose distribution before treatment. RECIST method and CTCAE method were used to evaluate the response and pulmonary toxicity after therapy.

Results: Median follow-up period was 3 months. The overall response rate was 85.7% (Complete Response: 28.6%, Partial Response: 57.1%) in 3 months after treatment. Radiation pneumonitis or pulmonary fibrosis was appeared in 5 patients but all pulmonary toxicities were less than grade III.

Conclusion: We can suggest that tomotherapy for pulmonary metastasis of breast cancer was a safe and effective treatment modality but we need further study about survivals, chronic complication and influencing factors through long term follow-up in larger group of patients to make up the limitation of our experience.

Breast Conserving Surgery (BCS) and Accelerated Partial Breast Irradiation (APBI) Using the Mammosite® Brachytherapy System for Early Breast Cancer: Initial Clinical Experience

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Purpose: To determine outcomes of this novel form of therapy in women undergoing BCS followed by APBI using the MammoSite® Brachytherapy Device.

Methods: Eligible participants were mostly postmenopausal patients: with favorable histopathology; with tumor size <3 cm; with contraindications to whole breast irradiation due to pulmonary problems or previous radiation to thorax. Sixty-eight patients were enrolled from June 2002 to July 2006. Because of seroma or 'air gaps', all but 18 patients had drain placement at the time of lumpectomy and device placement. A tumor dose of 340 cGy to 1 cm from the surface of the balloon, twice a day was delivered utilizing HDR Ir-192 for 5 consecutive days.

Results: The mean age was 65 years. All but 6 patients (2 T1s, 4 T2) had T1 disease. Fifty-eight patients had N0 disease. Five devices were explanted. The mean time to initiation of APBI in 18 patients without drain was 7.3 days (range 5-12) as compared to 4.98 days (range 3-7) in 47 patients who had drain placement (p=0.00005). Six patients developed delayed seroma requiring aspiration more than 6 months after treatment. One patient recurred 3 years after treatment. Two patients died of brain metastasis at 19 and 23 months. The majority of patients had excellent or good cosmetic results based on the Harvard Scale.

Conclusion: APBI using the MammoSite® Brachytherapy System is well-tolerated and has shown favorable outcomes. However, radiation treatment delay and infection are common; patients may warrant judicious use of drain placement and perioperative antibiotics.

The Implication of Hot Spots on Bone Scans within Irradiated Field for Breast Cancer Patients Treated with Mastectomy Followed by Radiotherapy

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Purpose: To analyze the implication of abnormal hot spots in the irradiated field of patients treated with mastectomy followed by radiotherapy for locally advanced breast cancer.

Methods: We reviewed 1,842 consecutive bone scans performed for 292 patients treated with modified radical mastectomy and followed by radiotherapy. If abnormal hot spots at irradiated sites were detected in bone scans, we evaluated further studies to determine whether bone metastases were present. Radiation was given using 4 or 6 MV X-rays at a dose of 50.4 Gy during 5.5 weeks with a dose per fraction of 1.8 Gy. Hormonal therapy was used in 171 of the (58.6%) patients. The follow-up period was 25-136 months (median: 57 months) from the date of the initial radiotherapy.

Results: During the follow-up, 60 patients (20.6%) developed bone metastasis. Solitary rib metastases were identified in four patients; all were detected outside of the irradiated field. Among 232 patients who did not develop bone metastasis, hot spots in the irradiated field were detected in 30 patients (12.9%). The cumulative incidence of hot spots at 5 years was 12.9%. The cumulative incidence of hot spot was more common in postmenopausal women, patients of less than 60 kg, patients with adjuvant hormonal therapy and patients irradiated including supraclavicular area.

Conclusion: We confirmed that the hot spots within the irradiated fields might be benign, especially in patients who were postmenopause, had a low body weight and received adjuvant hormonal therapy and irradiation that included the supraclavicular area.

Adjuvant Radiotherapy after Breast Conserving Surgery: Changes of Strategy on the Regional Nodal Irradiation over 10 Years

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Purpose: To evaluate the value of regional nodal irradiation (RNI) in breast cancer patients who had breast conservative treatment.

Methods: 407 patients, who underwent postoperative radiotherapy after breast conserving surgery for infiltrative breast cancer from November 1992 to January 2002 were enrolled. Whole breast irradiation (WBI) alone was given to patients with N0 (297 patients) or Nx (14 patients). For patients with 1-3 positive lymph nodes (LN's) (76 patients), three different strategies on the RNI were applied. Between November 1992 and October 1995 (Period I), patients had RNI including axillary, supraclavicular, and internal mammary LN. Between November 1995 and October 1995 (Period II), the extent of RNI was reduced to axilla and supraclavicular fossa. Between November 1996 and January 2002 (Period III), no RNI was given. Patients with >4 lymph nodes (20 patients) had RNI + WBI from Period I to III.

Results: There were 7 regional recurrences: 6 in supraclavicular LN, one in axillary LN. The 5-year regional failure rates of patients with N0, Nx, 1-3, and >4 LN's were 1.0%, 7.1%, 1.3%, and 7.1%, respectively ($p=0.4320$). Among patients with 1-3 LN's, only one patient had a regional relapse in the supraclavicular fossa, where RNI was not given. However, there was no difference in the 5-year regional failure rate among 3 Periods: 0%, 0%, and 2.0% for Periods I, II, and III, respectively ($p=0.7711$).

Conclusion: Omitting regional nodal irradiation in patients with 1-3 LN's did not result in increased regional failure.

The Effect of Dance and Movement Therapy on Patients with Breast Cancer

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Purpose: The purpose of this study was to examine the effect of dance and movement therapy (DMT) on the quality of life, depression, stress hormone, immunity and heart rate variability in patients with breast cancer.

Methods: The subjects are 52 patients with breast cancer who completed surgery and adjuvant therapy more than 2 years ago at the Department of Surgery from at Wonkwang University Hospital. Seventeen patients of subjects were selected according to the patients' informed consent of participation in DMT. The patients completed 14 weeks treatment program which was compose of 180 minutes session per week. BDI, STAI, VAS, SSI, CCQ, SSRS and biological parameters were compared before and after dance and movement therapy.

Results: The DMT for 14 weeks significantly results in the decrease depression, and increase role physical and general health perception of SF-36-K. The DMT for 14 weeks significantly increased level of T cell and T helper cell, and significantly decreased norephinephrine level. The DMT for 14 weeks significantly increase Standard Deviation NN interval (SDNN) and TP in HRV.

Conclusion: These result suggest that depression could be evaluated and treated in patients with breast cancer, and the DMT could be considered as a treatment program for patients with breast cancer.

Phase II Study of Primary Chemotherapy with Paclitaxel Plus Gemcitabine in Patients with Stage II and III Breast Cancer

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Purpose: Clinical outcomes were superior by adding gemcitabine (G) to paclitaxel (P) compared with P alone in metastatic breast cancer (BC). This study evaluated clinical and pathological response rates and adverse events by primary chemotherapy with P and G in stage II and III BC.

Methods: Patients (pts) with histologically confirmed stage II and III BC with positive axillary nodes by PET or positive FNA under sono guidance were eligible. Pts received P 80 mg/m² and G 1,200 mg/m², intravenously, d1/d8 every 3 weeks × 4. Postoperatively, doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m², intravenously, d1 every 3 weeks × 4 were given followed by radiation therapy.

Results: All planned 44 pts were enrolled. The median age was 43 years (range, 30-72 years) and the median primary tumor size was 5.5 cm (range, 2.1 to 12.4 cm). Thirty tumors (68%) were ER or PR positive and 32%, HER2 IHC 3+. Clinical responses were 1-CR (2%), 34-PR (77%), 7-SD (16%) and 1-PD (2%). 43 pts underwent surgery with 28 (65%) breast conserving surgery. Eight pts achieved pathologic CR in primary tumors (18%), 11 in axillary nodes (25%), and 5 in combined tumor and axillary nodes (11%). Grade III/IV toxicities were neutropenia (57%), leucopenia (14%), febrile neutropenia (2%), and headache (2%).

Conclusion: Preoperative P and G combination is well tolerated and effective for stage II and III breast cancer. Supported in part by NCC Grant No. 06102240-2 and SHIN POONG PHARM CO., LTD. which provided paclitaxel and gemcitabine.

The Effect of Aromatase Inhibitors on Recovery of Ovarian Function in Young Patients with Breast Cancer

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Purpose: The benefit of aromatase inhibitors (AIs) as adjuvant therapy in menopausal patients with hormone receptor positive breast cancer has been proven. However, the effect and safety of AIs in young breast cancer patients with chemotherapy induced amenorrhea has yet been established. The goal of this study was to evaluate the indications of AIs in these patients.

Methods: From December 2000 to December 2006, fifty-eight patients with hormone receptor positive tumor under the age of 45 were included in this study. All patients were amenorrhea status after chemotherapy and treated with AIs. Age of the patients, type of chemotherapy, and status of ovarian function recovery were analyzed according to medical records.

Results: Recovery of ovarian function was observed in 16 patients (27.6%). Among these patients, 13 renewed menses, and 3 were biochemically premenopausal status. The mean duration for ovarian function recovery after the use of AIs were 7 months. Patients younger than 40 years significantly more recovered from amenorrhea than older patients ($p=0.015$). Patients showed signs of ovarian function recovery is smaller in group treated CMF regimen (9/44, 20.5%) than in group treated anthracyclin-based regimen (7/14, 50.0%) ($p=0.043$).

Conclusion: AIs need to be used with caution in young women with chemotherapy induced amenorrhea. Patients under the age of 40 or those treated with anthracyclin-based chemotherapy must be carefully considered possibility of ovarian function recovery before using AIs. Use of AIs as adjuvant therapy in these patients with chemotherapy induced amenorrhea may promote unwanted recovery of ovarian function.

Serum Levels of Tartrate-Resistant Acid Phosphatase-5b in Breast Cancer Patients with Bone Metastases

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Purpose: Bone metastases are common in patients with advanced breast cancer. The serum levels of pyridinoline cross-linked carboxy-terminal telopeptides of type I collagen (I-CTP) have been used as a marker for breast cancer patients with bone metastases. The serum levels of a bone resorption marker, tartrate-resistant acid phosphatase (TRAP)-5b, were compared with those of I-CTP in patients with breast cancer.

Methods: The serum levels of TRAP-5b and I-CTP were simultaneously measured using their respective ELISA assays in 106 breast cancer patients with (n=45) or without (n=61) bone metastases. The relations of their values to clinico-pathologic factors, in particular, the presence or absence of bone metastases, were investigated.

Results: The serum TRAP-5b levels were higher in patients with intermediate or severe bone metastases than in those without bone metastases ($p < 0.0001$). The serum levels of TRAP-5b correlated with those of I-CTP ($p < 0.0001$). An ROC analysis resulted in a cut-off value for TRAP-5b of 2.8 U/L for the detection of bone metastases, showing it to have a sensitivity of 40% and a specificity of 83.6%. The serum TRAP-5b levels were lower in patients receiving bisphosphonate with severe bone metastases than in those not receiving bisphosphonate ($p = 0.04$). Changes in the serum TRAP-5b levels during treatments correlated with those of serum CA 15-3.

Conclusion: The specificity of serum TRAP-5b levels for the detection of bone metastases was relatively high but its sensitivity was low. Serum TRAP-5b levels may be useful for the evaluation of osteolytic changes in bone metastases.

Preliminary Study of Serum HER-2/neu Concentration in Korean Breast Cancer

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Purpose: We evaluated them if serum HER-2/neu concentration is a valid index of HER-2 status among women with Korean primary breast cancer.

Methods: Serum HER-2 levels were examined among 131 female patients with breast cancer. Serum Her-2/neu levels were measured by Chemiluminescence immunoassay (ADVIA centaur system) during preoperative period. All breast cancer tissues were tested by IHC for HER-2/neu, and underwent FISH analysis for IHC+2. When IHC+3 or FISH amplified, we concerned it as HER-2/neu overexpressed breast cancer. The cut-off value was 10.2 ng/mL.

Results: HER-2/neu overexpressed patients were 58 patients (20.3%) in IHC or FISH. Median serum Her-2/neu level was 10.5 ng/mL (± 4.02). Node positive breast cancer were 108 patients (37.8%). 97 patients showed hormone responsive breast cancers (73.5%). Median tumor size of invasive tumor was 2.3 cm (± 1.4). Serum HER-2/neu concentration was significantly correlated with HER-2/neu positive breast cancer (HER-2/neu not overexpressed vs expressed, 9.26 ng/mL vs 12.7 ng/mL $p < 0.001$). Increased serum HER-2/neu levels were associated with lymph node status ($p = 0.036$) and hormone unresponsiveness ($p = 0.010$), tumor size ($p = 0.049$), and CA 15-3 ($p < 0.001$) however not associated with age and CA15-3. Serum concentration more than 10.2 ng/mL was 122 patients. Patients of serum HER-2/neu above 10.2 ng/mL showed higher frequent hormone receptor negative and nuclear grade, but not associated with EGFR-1 amplification, p53, and CD5/6.

Conclusion: Serum HER-2/neu was relatively correlated with tissue HER-2/neu expression in HER-2 overexpressed breast cancer. It is associated with tumor size, lymph node metastasis status, CA15-3. Serum HER-2 is necessary to assess as the tumor marker in primary breast cancer and various clinical field of breast cancer.

Clinical Value of Serum Tumor Marker CEA, CA 15-3, and TPS in Recurrence of Breast Cancer

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Purpose: The aim of this study was to compare the value of serum tumor marker CEA, CA 15-3, and TPS with other prognostic factors of breast cancer and to consider the effectiveness of these serum markers in detection of recurrence of breast cancer.

Methods: Blood samples from all patients with breast cancer were done before surgery. Serum tumor markers were serially checked during follow-up period. The values of tumor markers were compared with other prognostic factors of breast cancer.

Results: Of those three markers, the median concentration of CA 15-3, checked before surgery, was higher in patients with LN positive, large tumor size (larger than 5 cm), and high grade tumor. The status of ER, PR, and HER-2/neu were not correlated with tumor markers. In detection of recurrence, the TPS had the greatest sensitivity (72.7%). However, the CA 15-3 had the highest specificity (98.7%). The positive predictive values were 50% for CEA, 84.6% for CA 15-3, and 30.8% for TPS. The negative predictive values were 84.7, 85.9, and 94.6%, respectively. Combined evaluation of those three tumor markers did not increased sensitivity in detection of recurrence. In the ROC curve analysis, TPS had the largest area (0.795) under the curve.

Conclusion: CA 15-3 was correlated with other prognostic factor of breast cancer. Pre-operative concentrations of serum level of CEA, CA 15-3, and TPS had no implication in recurrence of breast cancer. TPS is the most useful serum tumor marker in detection of recurrence of breast cancer.

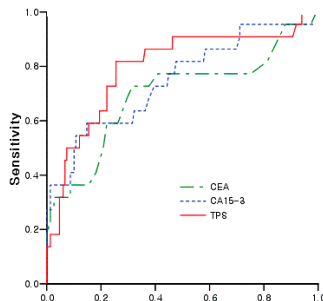


Fig 1. Receiver operating characteristic (ROC) curves.

Evaluation of Novel Molecular Markers for the Detection of Breast Cancer Cells in Peripheral Blood

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Purpose: Molecular detection of breast cancer cells in peripheral blood can be useful for optimizing individualized treatment and early detection of recurrence. Cytokeratin 19 (CK19) has been known as an epithelial cell marker. BU101 and BS106 are breast-specific markers recently reported by researchers in Duke University. The aim of this study is to evaluate the clinical utility of these three markers for the detection of occult breast cancer cells in peripheral blood.

Methods: 3 mL of EDTA-anticoagulated blood from 34 breast cancer patients and 18 non-cancerous women were assayed. We separated mononuclear cells from whole blood and extracted RNA. Quantitative real-time RT-PCR assays were performed with 4 molecular beacon probes (CK19, BU101, BS106 and beta2 microglobulin). We used SK-BR3 to construct a standard curve for each marker.

Results: Out of the 34 breast cancer patients assayed, 9 (26.5%) had detectable CK19 expression and 6 (17.6%) had BS106. One breast cancer patient who had both CK19 and BS106 expression has shown to have bone marrow metastasis. Out of 18 non-cancerous women, CK19, BU101 and BS106 were detected in 3 (16.7%), 1 (5.6%) and 6 (33.3%) respectively. CK19+BS106 and BU101+BS106 expressions were detectable in 1 specimen each. No breast cancer or non-cancerous specimen showed detectable expression in all three markers.

Conclusion: Although BS106 was expressed in non-cancerous women, a combination of three markers (CK19, BU101 and BS106) can be a potential marker to detect occult breast cancer cells in blood. Further evaluation with a large number of specimens and long-term follow up would be needed.

DNA Methylation Profiles and Field Cancerization in Breast Cancer

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Purpose: Epigenetic alterations, represented by aberrant DNA methylation, are deeply involved in human cancers. The aim of this study was to determine DNA methylation pattern and to identify epigenetic biomarkers frequently hypermethylated in histologically normal tissues from multiple geographic zones adjacent to primary breast tumors.

Methods: We used HpaII-MspI-PCR to explore methylation profiles of 50 tumor suppressor genes in breast cancer. We first determined methylation status of 50 genes in two breast cancer cell lines MCF7 and MDA-MB231 and 8 genes (APC, CALCA, CDH13, EDNRB, H19, MTHFR, MUC2, S100A2) were found to be methylated in at least 1 cell line. Secondly, we analyzed methylation status of these 8 genes in 36 breast cancer patients. To examine field cancerization effect of 8 genes in grossly normal appearing tissues, we tested methylation status in paired tumor adjacent tissues with different distance away from tumor tissues in 7 patients.

Results: Methylation frequency of five genes is determined as follows: MTHFR (47.2%), APC (55.6%), EDNRB (69.4%), CALCA (77.8%), S100A2 (88.9%), CDH13 (88.9%), H19 (94.4%) and MUC2 (97.2%) respectively in breast cancer. Six (MUC2, H19, MTHFR, S100A2, CALCA, CDH13) out of 8 genes were methylated in normal appearing tissue even 8cm away from the tumor.

Conclusion: Detection of DNA methylation pattern and complementary molecular assessment of tumor margins should be useful in early cancer detection, risk assessment and definition of tumor margins.

Overexpression of Interleukin-10 in Sentinel Lymph Node with Breast Cancer

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Purpose: In breast carcinoma, identification of tumor cells in the sentinel lymph nodes is a predictor of the tumor's metastatic potential. Sentinel lymph node may be targeted not only by tumor cell metastasis but also by cytokines from the emergence of anti-tumor immune responses.

Methods: Between February 2003 and February 2004, the investigator evaluated 38 cases that underwent sentinel lymph node biopsy at Samsung Medical Center. Eighty paraffin-embedded sections, 49 sentinel and 31 non-sentinel lymph node, from breast carcinoma without lymphatic metastases were analyzed by real time polymerase chain reaction to evaluate the cytokine profile (interferon- γ , interleukin-2, interleukin-10 and interleukin-12 for the T cell response).

Results: A higher expression of interleukin-10 was observed in sentinel lymph node than in non-sentinel lymph node ($p=0.03$). The expressions of interferon- γ , interleukin-2 and interleukin-12 were similar between sentinel and non-sentinel lymph node.

Conclusion: Overexpression of IL-10 in SLNs was observed from breast cancer without lymph node metastasis. This result showed some immunologic difference between SLNs and non-SLNs. We proposed that the immunologic suppression of SLNs in breast cancer without lymph node metastasis. This result suggests the distinct characteristics of SLN not only anatomically but also immunologically. Further analysis for micro-environment of immunologic system will be needed to clarify the role of SLN and design immunotherapy for SLN in breast cancer patients.

Prognostic Comparison of Sentinel Lymph Node Biopsy with Axillary Lymph Node Dissection in Node Negative Breast Cancer Patients

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Purpose: Sentinel lymph node biopsy (SLNB) is replacing ALND as the axillary staging procedure in breast cancer patients with clinically negative axilla. However, it is unclear whether this influences patient survival. Our aim was to compare the survival of node-negative patients who received only SLNB to that of node-negative patients who received routine ALND.

Methods: We reviewed the records of 554 node negative breast cancer patients who treated at our hospital from 1995 to 2005. Survival was compared between SLNB group (n=124) and ALND group (n=430) with at least 10 axillary nodes removed.

Results: The median follow up was 49.0 months and the median disease free survival was 34.0 months. The mean age was 48.28 years and younger (<35) vs. older (≥35) patient's proportion was no difference between two groups (p=0.136). The mean tumor size was 2.21 cm and there was no significant difference in distribution of tumor size (pT), stage and hormonal receptor status between the two groups (p=0.121, p=0.057, p=0.106). The distribution of c-erbB2- overexpression, mastectomy and adjuvant systemic therapy within the two groups showed significant difference (p=0.000, p=0.000, p=0.000) with a higher percentage in ALND group. Recurrences were found 46 patients (10.7%) in ALND group and 2 patients (0.6%) in SLNB only group (p=0.002). Locoregional recurrences were detected only in 18 patients (40%) in ALND. Disease free survival rate at 3 year was 89.2% in the ALND groups and 98.3% in the SLNB group, there was no significant differences between two groups (p=0.148).

Conclusion: Although our report is short-term result, SLNB appears to be a safe and reliable procedure for axillary staging and to ensure locoregional control in SLN-negative breast cancer.

Evaluation of Axillary Lymph Node Status with Imaging and Cytology

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Purpose: Sentinel node biopsy (SNB) has become a new standard of care for patients with clinically node-negative early stage breast cancer in the recent years. This procedure is very beneficial for the patients, but we should avoid not only “unnecessary lymph node dissection,” but also “unnecessary SNB.” So we performed imaging studies (CT and US) and fine needle aspiration cytology (FNAC) for more accurate evaluation of axillary lymph node (AxLN) status.

Methods: 424 female patients with clinically node-negative T1-T2 breast cancer who underwent the SNB procedure were reviewed. All patients underwent multi-detector CT (MDCT) of axilla and breast preoperatively. Contrast-enhancement study was performed and then 3dimensional (3D) images were reconstructed. Axillary US were also performed in all patients and fine needle aspiration cytology was done if lymph node swelling was detected. If cytological examination was revealed to be negative, SNB was performed.

Results: Negative predictive value of axillary CT was 84.5%. The accuracy of cytological examination of AxLN was 80%. Among the cytological node-negative patients, incidence of axillary node involvement in pathological examination was 21.3%. But most of these patients had only one positive node. 60 of 424 patients (14%) have positive nodes and underwent axillary dissection.

Conclusion: Many studies presented that node-positive rate of SNB was approximately 30%. In the present study, node-positive rate was 14%. 3D-CT imaging and US guided FNAC of AxLN were useful for more accurate selection of candidate for SNB.

Significance of Preoperative Fluorodeoxyglucose-PET for Detection of Axillary Lymph Node Metastasis

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Purpose: The axillary lymph node status is still considered the single most important prognostic indicator in patients who have breast cancer. Clinical examination is generally unreliable for staging the axilla. Lack of conventional imaging techniques to determine the axillary lymph node involvement with acceptable accuracy has been the main reason for axillary lymph node dissection. Metabolic imaging with FDG-PET is suggested to provide more specific information, based on detecting increased glucose consumption of cancer tissue. This study was undertaken to evaluate the diagnostic accuracy of preoperative positron emission tomography.

Methods: A retrospective review from January of 2007 to July of 2007 was performed in all patients (n=45) undergoing a preoperative FDG-PET. PET imaging with the radiolabeled glucose analogue (F-18 FDG) was used to visualize the primary breast tumor and metastatic lesions.

Results: In 45 patients, the sensitivity and specificity of PET for detection of axillary lymph node metastasis were 70% and 91.4%, respectively. Overall accuracy was 86.7%. In patients (n=15) who had primary breast tumors larger than 2 cm (>stage pT1), the sensitivity increased of 100%, with corresponding specificity of 100%.

Conclusion: FDG-PET cannot replace the axillary dissection, not only because of the limited sensitivity, but also because the number of involved lymph nodes and extranodal extension cannot be determined. But, among patients who have larger tumors, sentinel biopsy can be avoided in those who have positive FDG-PET, in whom complete axillary lymph node dissection should be the primary procedure.

Sentinel Lymph Node Biopsy before Primary Treatment for Axillary Lymph Node Staging in Breast Cancer

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Purpose: In the management of early-stage breast cancer, estimating the relapse risk is important before starting the treatment. We performed sentinel lymph node biopsy prior to any treatment for the patients with clinically node-negative breast cancer to decide whether primary chemotherapy or primary surgery.

Methods: The sentinel lymph node biopsy was performed under local anesthesia and out-patient setting. The sentinel lymph nodes were identified with 99m technetium-labeled phytate and patent blue dye. We performed pre-treatment sentinel lymph node biopsy in 174 breast cancer patients.

Results: A mean of 1.8 sentinel lymph nodes were identified and the detection rate was 100%. Forty-six (26.4%) patients showed positive sentinel lymph node for metastasis. Finally, 42 (24.1%) patients underwent primary chemotherapy followed by surgery. For patients with negative sentinel lymph node for metastasis, surgery only to the breast and following systemic therapy was applied according to the clinicopathologic characteristics of the primary tumor. We performed axillary lymph node dissection in 38 patients. Thirteen (34.2%) patients had residual nodal disease.

Conclusion: Sentinel lymph node biopsy before primary treatment is practical for precise risk assessment and could be available for deciding therapeutic pathway.

New One-Step Nucleic Acid Amplification (OSNA) for Intra-Operative Detection of Lymph Node Metastasis in Breast Cancer Patients: Multi-Institutional Clinical Study

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Purpose: Accurate intra-operative detection of axillary (Ax) lymph node (LN) metastasis status is essential for appropriate dissection in the breast cancer operation. Based on the preliminary study of LN metastasis detection system by OSNA with cytokeratin (CK) 19 mRNA, multi-institutional clinical study was conducted to evaluate its diagnostic reliability.

Methods: Two protocols were applied. Protocol 1; false-positive rate of OSNA assay was evaluated. Clinically negative AxLNs were divided into 4 blocks with 2 mm thickness. Two alternate blocks were used for OSNA, the remaining blocks for serial slicing at 0.2 mm intervals for H&E and CK19-IHC (immunohistochemical) staining. Protocol 2; concordance rate was evaluated between OSNA and the 3-level histopathological examination. AxLNs were divided into 4 blocks with 2 mm thickness. Two alternate blocks were used for OSNA, the remaining blocks for histopathological examination; 3 cutting surfaces of the remaining 2 blocks were examined for H&E and CK19-IHC staining.

Results: Protocol 1; 141 AxLNs from 37 patients were examined. 125 AxLNs were negative by both OSNA and histopathology (specificity = 96.9%, 95% CI: 0.923-0.993). Protocol 2; 469 AxLNs from 175 patients were examined. The positive rate was 14.1% by histopathology and 16.0% by OSNA. Fifty-four AxLNs were positive and 382 were negative by both methods (concordance rate = 93.0%, 95% CI: 0.903-0.951).

Conclusion: OSNA consistently gave nearly the same results as those of the 3-level histopathological examination for each LN used in this study. These results suggested OSNA would be an alternative tool for intra-operative detection of lymph node metastasis.

The Significance of Sentinel Lymph Node Biopsy in Patients with Ductal Carcinoma In Situ and Ductal Carcinoma In Situ with Microinvasion of the Breast

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Purpose: The purpose of this study is to determine the prevalence of sentinel lymph node metastases in ductal carcinoma in situ (DCIS) patients and to evaluate the clinical usefulness of the SLNB.

Methods: Between December 1998 and September 2004, 41 patients who underwent SLNB for DCIS at the Department of Surgery, Yongdong Severance Hospital were reviewed retrospectively. The excised sentinel lymph nodes were examined by frozen section, by H&E stain, by cytokeratin immunohistochemical (IHC) stains. Clinicopathological data were analyzed and compared with sentinel lymph node status.

Results: SLNB was performed in 41 patients with 42 cases of DCIS (one patient with bilateral disease). Of 29 cases were pure DCIS and of 13 cases were DCIS with microinvasion (DCISM). There are no metastatic sentinel nodes in pure DCIS patients. Three cases (23%) of DCISM had isolated tumor cells in their sentinel nodes. All three positive sentinel nodes were detected only by IHC stains. Further axillary dissection was performed in three patients but no positive nodes were found in all cases. During 26.5 months mean follow up period (5-62 months), one case with DCISM recurred in the liver 37 months after operation who had isolated tumor cells in sentinel lymph node. But there is no locoregional recurrence in this patient.

Conclusion: Based on our data, SLNB may not be routinely performed for patients with DCIS. However, in the patients with DCISM, SLNB may be considered for the evaluation of axillary status.

Early Diagnosis of Breast Cancer by Wire Localisation and Biopsy – A 10 Year Review of 342 Patients

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Purpose: More and more non palpable lesions are detected with by mammography. Diagnosis of early breast cancers has been increased through bBiopsies of these clinically occult lesions have resulted in increased numbers of diagnosed early breast malignancies. There are many many minimally invasive biopsy methods of minimally invasive strategies to obtain histological diagnosis, with the help of different various imaging modalities. We evaluated our experience of wire localisation localization and biopsy of nonpalpable breast lesions done in our department to see if there was still a role for this procedure.

Methods: We retrospectively reviewed the clinical records, mammograms and the histological diagnosis of 342 consecutive patients who underwent wire localiszation in during a 10 year-period from between January 1997 to and October 2006.

Results: A total of 358 wire localizations were performed. The mean age of the patients was 50 years (range 30-79 years) at the time of wire localisationlocalization. A total of 358 wire localisations were performed. Eight patients had underwent the procedure done for both breasts lesions in the same setting, while and 8 others patients underwent for aon separate caseoccasions. The overall malignancy rate was 24% (86/358). The most common benign finding [59.2%, (212/358)] was fibrocystic changes/disease at 59.2% (212/358). 0.001% (5/358) of the specimens were non diagnostic.

Conclusion: The results from this large retrospective review showed a comparable malignancy rate with other published data. There is still a diagnostic place role offor wire localisation localization and biopsy of for non palpable breast lesions for diagnosis and, in selected cases, as part of a therapeutic procedure in breast conserving therapy.

Contrast Enhanced MRI Findings of Ductal Carcinoma In Situ

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Purpose: The purpose of this study is to describe characteristic contrast enhanced MR mammographic findings of ductal carcinoma in situ (DCIS) and DCIS with microinvasion.

Methods: From January 2000 to March 2007, 46 women with 47 lesions affected by proved to be a DCIS or a DCIS with microinvasion were underwent contrast enhanced MRI and were retrospectively evaluated. All patients underwent were submitted previously to mammography and breast ultrasonography. All findings of mammography, breast ultrasonography (US), and MRI were analyzed by ACR BI-RADS lexicon.

Results: All 47 cases lesions were enhanced under theon enhanced MR images. Smooth margined homogeneous enhanced mass was seen in the eight (8/47) cases lesions and nonmass enhancement was seen in the 39 (39/47) lesionscases. Among non-mass enhanced lesionsment, focal enhancement (8/39), ductal enhancement (6/39), segmental enhancement (12/39), and regional enhancement (13/39) were observed. In kinetic analysisstudy, wash-out pattern (18/47), plateau pattern (26/47), and persistent pattern (3/47) were demonstrated. No significant differences were noted between pure and microinvasive DCIS.

Conclusion: There is no significant difference between pure and microinvasive DCIS in contrast enhanced dynamic breast MRI. However, contrast enhanced MR images can demonstrate occult foci, multifocal lesion, and tumor extent of DCIS on mammogram or ultrasonogram.

Feasibility of Dynamic Enhanced MDCT in the Differentiation of Malignant and Benign Breast Lesions

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Purpose: The purpose of our study was to evaluate the usefulness of dynamic enhanced multidetector-row computed tomography (MDCT) in differentiating the malignant and benign breast lesions.

Methods: Thirty-eight breast cancer patients (age range: 34-75 years, mean 51.3 years) were examined underwent preoperative dynamic CT scan using MDCT protocol which consists of, in which pre-contrast, early arterial (30 seconds), late arterial (60 seconds), and delayed phase (180 seconds) scan was checked after rapid injection of contrast media (3.5 mL/s). The CT values (Hounsfield unit, HU) and enhancement patterns of malignant lesions (n=41) were compared with those of benign lesions (n=12). The CT values (HU) of malignant breast lesions were compared with intratumoral microvessel density (MVD) for assessing the tumor angiogenesis.

Results: Mean CT values (HU) of malignant lesions (n=41) were 37.8±7.9, 91.3±20.6, 123.6±26.2, 120.9±18.7 in each pre-contrast, early arterial, late arterial and delayed phases. Mean CT values (HU) of benign lesions (n=12) were 30.6±14.6, 66.6±22.2, 92.4±23.7, 106.3±21.1, respectively. The CT values (HU) of malignant lesions were higher than those of benign lesions in early and late arterial phases (p<0.001). The cut-off points were determined to be 75 HU in the early arterial phase (83% sensitivity, 58% specificity) and 105 HU in the late arterial phase (80% sensitivity, 75% specificity). The MVD of the malignant breast lesions was 19-138 (mean 78.3±25.0). The correlation between CT values (HU) and MVD of malignant breast lesions was fair on late arterial phase (correlation coefficient = 0.437, p<0.01).

Conclusion: The analysis of enhancement features on dynamic MDCT can help to differentiate malignant and benign breast lesions.

Clinical Utility of MRI before Re-lumpectomy in Breast Cancer Operation

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Purpose: The purposes of this study were to assess the accuracy of breast MRI in detecting residual tumor extent and to evaluate the role/impact of breast MRI for surgical treatment planning.

Methods: Preoperative breast MRI was performed in 47 breast cancer patients who had underwent mammotome biopsy and or excisional biopsy with unknown resection margin status. All subjects underwent breast MRI and ultrasonography performed by experienced radiologist for the evaluation of extent of residual tumor, and were evaluated by experienced diagnostic radiologist, followed then underwent by immediate curative operation. We examined the evaluated correlation between radiologic and pathologic finding.

Results: Residual tumor was present in 33 patients (70.3%) and multifocal breast cancer was found in 12 patients (25.5%). In terms of the accuracy of MRI in detecting residual tumor, the sensitivity was 63.6%, specificity was 45.5% and the positive predictive value was 77.7%. Pathologic finding of residual tumor showed that ductal carcinoma in situ was most common (57.1%) in not only radiologic-pathologic concordant cases, but also in radiologic-pathologic discordant cases (58.3%). The MR findings of residual tumor changed the next procedure from re-lumpectomy to mastectomy (10 patients), additional biopsy of suspicious lesion in ipsilateral breast (2 patients), and second-look ultrasonography (4 patients).

Conclusion: In assessing the diagnostic accuracy of MRI in showing the presence and extent of residual tumor, we found that MRI had sensitivity, specificity and accuracy of 63.6%, 45.5%, and 77.7% respectively. An important clinical role of MRI is to identify a subset of patients with extensive residual or multifocal breast cancer who would be better served by undergoing mastectomy rather than breast conserving operation.

The Clinical Significance of Preoperative MRI for Determination of Surgery in Breast Cancer

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Purpose: Currently MRI is widely used for the preoperative staging of breast cancer. In this study, We assessed the impact of preoperative breast MRI for determination of surgical extent in on the surgical management of breast cancer patients in women.

Methods: From March 2004 to October 2006, 162 cases patients underwent were enrolled for preoperative MRI for the staging of breast cancer. The MRI findings and clinicopathological results were investigated and the accuracy of breast MRI was analyzed with respect to the detection of multiplicity, nipple involvement and bilaterality of the breast cancers.

Results: For detecting multifocal lesions, the sensitivity and specificity of breast MRI were 100% and 48.5%, respectively, and the results of breast US were 100% and 63.4%, respectively. For detecting nipple invasion, the sensitivity and specificity of breast MRI was 80% and 74.6%, and for those of breast US were 33.3% and 86.4%. In 27 cases (16.7%), the type of surgery was changed according to the preoperative MRI findings. However, in only 6 cases, were the MRI findings in were concordant with the pathological findings of the mastectomy specimen.

Conclusion: In clinical application of breast MRI for preoperative staging, the decision to undertake surgery for breast cancer based on a MRI findings should be prudent due to its specificity.

Factors That Can Predict Invasive Component of DCIS Diagnosed by Ultrasound-Guided Core Needle Biopsy

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Purpose: To investigate factors associated with predicting the presence of invasive carcinoma components within final specimens initially diagnosed with DCIS by ultrasound-guided CNB.

Methods: Data from 174 women with an initial core needle biopsy (CNB) diagnosis of DCIS who underwent surgical resection from January 2000 to January 2007 were retrieved from our database. Patients clinical characteristics, pathologic data, and mammographic and ultrasound data were prospectively recorded into a computer database, and a retrospective review was then performed. CNBs were performed with a 11-gauge vacuum assisted core biopsy needle or a 14-gauge automated needle under only ultrasound guidance.

Results: In univariate analysis, the rate of upstaging to invasive carcinoma on final pathology was associated with the abnormal palpation on physical examination ($p < 0.001$), BI-RADS C5 ($p = 0.006$), and 11 gauge vacuum assisted CNB procedure ($p = 0.013$). However age, mammographic mass, ultrasonic mass, microcalcification, grade, and comedonecrosis were not associated with DCIS underestimation. Multivariate logistic regression analysis showed that abnormal palpation on physical examination and BI-RADS C5 were independent predictors for the presence of invasive carcinoma components within final specimens (odds ratio[OR] = 2.878; $p = 0.006$ and OR = 2.980; $p = 0.009$ respectively). Of the 71 patients with palpable mass, 45 (63.4%) had invasive cancer on final pathology review. Of the 44 patients with radiological assessment of BI-RADS C5, 28 (63.6%) had invasive cancer on final pathology review.

Conclusion: Palpation of mass and BI-RADS C5 can be significant and practical pre-operative predictors for invasive component within final specimens in patients with CNB diagnosis of DCIS under ultrasound guidance.

Computer-Aided Analysis of Delayed Enhancement Pattern in Dynamic Breast MRI; Correlation with the Histologic Grade of Invasive Cancer

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Purpose: To evaluate the value of computer-aided analysis of delayed enhancement pattern in dynamic breast MRI and to correlate the pattern with histologic grade of invasive cancer.

Methods: Twenty-nine invasive breast cancers were selected retrospectively from a series of contrast-enhanced dynamic MRI (IV injection of 0.1 mmol/kg of gadolinium-DTPA, Siemens Sonata 1.5T, T1 3D FLASH, fat saturation, sagittal, 170×170, 1 mm thickness, one pre-contrast, and four post-contrast phases; P1 to P4). The median longest diameter of tumors was 2.0 cm (range 0.9-4.0 cm). The maximum signal intensity (SI) of 64 (4×4×4) voxels at P1 or P2 was automatically selected using computer-aided analysis. In the same voxels, the washout ratio was calculated ($(SI_{max} - SI_4/SI_1) \times 100$). The ratio was scored as follows; 1, < -20%; 2, -20~20%; 3, >20%. Relationship between the histologic grade and the scores of washout were evaluated by means of linear regression.

Results: The histologic grade of invasive cancers was I in 6 (20.7%), II in 11 (37.9%) and III in 12 (41.4%). The scores of washout ratio was 1 (16.7%, 1/6), 2 (66.6%, 4/6) and 3 (16.7%, 1/6) in grade I cancers, 1 (0%, 0/11), 2 (63.6%, 7/11), 3 (36.4%, 4/11) in grade II cancers, and 1 (0%, 0/12), 2 (41.7%, 5/12), and 3 (58.3%, 7/12) in grade III cancers. The histologic grade had positive correlation with the washout ($p=0.037$).

Conclusion: The delayed enhancement pattern of dynamic breast MRI can be automatically analyzed by computer-aided program and the washout correlated with high histologic grade.

Computer Aided Quantification of Real-Time US Elastography: Differentiation of Benign from Malignant Nonpalpable Breast Masses

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Purpose: To retrospectively evaluate the diagnostic performance of US elastography for the differentiation of benign from malignant nonpalpable breast masses.

Methods: Real-time US elastography was performed in 140 women (mean age, 47 years; age range, 24-67 years) who had been scheduled for US-guided core biopsy of the nonpalpable breast masses (100 benign, 40 malignant). Representative images more than 2 planes were saved as a bitmap file. An experienced radiologist provided an elasticity score. Quantification of US elastography was obtained with a readily available software program. After subtraction gray scale images from elasticity images, a region of interest drawn around the mass on gray scale images was loaded on subtracted color-scale images. The score of each pixel ranged from red for greatest strain as 0 to blue for no strain as 255. Average, skewness, kurtosis, difference histogram variation (DHV), edge density (ED), and RUNLEN within a ROI were calculated. A multilayer perceptron neural network was used as classified.

Results: Mean value of elasticity score were 3.7 ± 0.8 (standard deviation) for malignant lesions and 2.5 ± 0.9 for benign lesions ($p<0.001$). Mean values of average, skewness, kurtosis, DHV, ED, and RULEN were significantly different between malignant and benign lesions ($p<0.01$ in all six features). Area under ROC curve (Az) values of elasticity score and neural network on the basis of all six feature values was 0.81 and 0.89 ($p<0.02$).

Conclusion: Computer aided quantification of US elastography may have a better diagnostic performance than real time US elastography for differentiation of nonpalpable breast lesions.

Inter- and Intraobserver Agreement in the Interpretation of Ultrasound (US) Elastography of Breast Lesions

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Purpose: To evaluate inter- and intraobserver agreement of breast radiologists for the visual assessments of strain images obtained with real-time free-hand US elastography.

Methods: During the last 5 months, 130 consecutive women (mean, 55 years; range, 27-78 years) who had been scheduled to undergo US-guided core biopsy were examined with a commercialized US elastography. BIRADS category based on gray-scale US was 3 in 15% (20/130), 4 in 62% (80/130), and 5 in 23% (30/130). Representative real-time gray-scale and elasticity image files were saved as video clips for a total of 130 lesions (80 benign, 50 malignant, mean size 1.2 cm, range 0.4-3.7 cm). Three experienced radiologists independently analyzed the video clips without knowledge of the histology and provided the elasticity score by 5-point scale according to the degree and distribution of strain induced by light compression. Results were evaluated by using weighted κ statistics and receiver operating characteristic (ROC) curve analysis.

Results: Three readers showed moderate to substantial interobserver agreement (mean κ ($m\kappa$), 0.644; range, 0.580-0.687) and substantial to almost perfect intraobserver agreement ($m\kappa$, 0.821; range, 0.742-0.918). Interobserver agreement of malignant lesions ($m\kappa$, 0.520; range, 0.480-0.583) was lower than that of benign lesions ($m\kappa$, 0.606; range, 0.520-0.668). There was no significant difference in inter- and intraobserver agreements according to lesion size. Mean area under the ROC curve was 0.817 (0.770-0.845, 95% confidence interval).

Conclusion: Interobserver agreement of breast radiologists was moderate to substantial and intraobserver agreement was substantial to perfect for the visual assessments of strain images obtained with real-time free-hand US elastography.

The Comparison of the Breast Ultrasound and MRI in Sizing and Detecting Breast Malignancies

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Purpose: Magnetic resonance imaging of the breast is increasingly used for the evaluation of tumor extent or the detection of additional multiple breast lesions. This study We compared breast MRI with and USUltrasound for the evaluation of tumor extent and detection of additional multiple breast lesionsin sizing breast lesions and detecting additional malignant lesions.

Methods: This studyWe reviewed the medical records of 145 patients who checked underwent both breast MRI and USUltrasound preoperatively in our institutionat Asan Medical Center betweenfrom January 2005 to December 2006. Those who had received initial Mammotomemammotome, excision or neoadjuvant therapy were excluded. Pathologic correlation was performed for the lThose lesions categorized as BI-RADS 4a VI-A or more on imaging were compared with the malignant lesions confirmed on pathology report.

Results: MRI of the breast is checked additionally due to diffuse microcalcification on MMG (29.8%), suspicious of multiple lesions on ultrasound (60.3%), proximity to nipple-areolar complex (6.6%), and occult or indefinite on USG (3.3%)The number of those lesions categorized as BI-RADS VI-A4a or more on US and MRI matched with the number of the malignant lesions confirmed on pathology report in 57% and 52.3% respectively (p=0.099). The size of the largest lesion measured on US and MRI matched with the size of the largest malignant lesion confirmed on pathology report in 57.6% and 50.3% respectively (matching criteria:size difference <0.5 cm, p<0.001). The direct comparison of lesions categorized as BIRADS VI-A or more on ultrasound and MRI lesions showed no mismatch (29.1%), size mismatch >0.5 cm (22.5%), number mismatch (23.2%), and size and number mismatch (25.2%).

Conclusion: MRI of the breast is useful and moer more accurate than ultrasound to evaluate the extent of the breast lesion and complementary to ultrasound to detect additional multiple breast lesions.

Subclassification of Birad Category 4 Microcalcification according to Morphologic Difference-More Accurate Method to Detect DCIS or Breast Cancer

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Purpose: We analyzed the morphologic features of microcalcifications using new scoring system to evaluate its ability to differentiate malignancy.

Methods: Total 87 cases were recruited for the study. They all received excisional treatment for non-palpable, mammographic BI-RADS category 4 microcalcifications. Mammographic morphologic features were analyzed and scored from 0 to 3 according to the severity for three categories (pleomorphism, linearity, clustering) by one breast radiology specialist. Scores for each category and total scores were compared to the pathologic result obtained after the operation.

Results: Malignant disease was diagnosed in 12 (13.8%) patients and 75 (86.2%) were diagnosed as benign disease. Three cases were invasive ductal carcinoma (IDC) and 9 cases were DCIS. Sixty eight cases were benign without atypia and most of them were fibrocystic diseases and 7 were atypical ductal hyperplasia (ADH). Total scores ranged from 1 to 7 in benign cases. In malignant cases, the score ranged from 3 to 9. There was a statistical significance between benign and malignant groups ($p \leq 0.0001$). Mean total scores were 3.3 in benign without atypia, 4.0 in ADH, 5.6 in DCIS and 7.3 in IDC ($p \leq 0.0001$). ROC curve analysis showed that the best cutoff value of total scores (4.5) was associated with a sensitivity and a specificity of 83% and 82%, respectively.

Conclusion: Our new scoring system can differentiate malignant microcalcifications more accurately than BIRAD classification. Before using our scoring system in clinical field, validation study should be preceded with different sets of cases.

A Novel Proposal for Earliest Diagnosing Cancer

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Purpose: To find the diagnosing cancers method in earliest stage of carcinogenesis.

Methods: By the scientific developments of cancer research, the author designed a proposal to diagnose cancers earliest.

Results: There are two kinds of antibodies to be used. One kind of antibody for this method (I-antibody) is produced by immunizing one kind of Rb gene or p53 gene exon expressed peptides respectively which is the most difficult one to be abnormality or no abnormal peptides at anytime. While the second kind of antibody (II-antibody) is produced by immunizing one kind of Rb gene or p53 gene exon expressed peptides respectively which is the most easily abnormal peptides. Using Rb's I-antibody and Rb's II-antibody, respectively, reacts at the same time with the suspected cancer specimen Rb genes expressed the same amount of Rb proteins. At the same time, Using p53's I-antibody and p53's II-antibody, respectively, reacts at the same time with the suspected cancer specimen p53 genes expressed the same amount of p53. Which all are immune reactions of antigens and antibodies and which the Rb proteins and p53 are labeled by radioisotope radio-sulfurs or radioisotope radio-iodium. Then tests the intensity of radioactivity of Rb proteins and p53 using the proper technology respectively. So that can analyse if the structures of the Rb proteins and p53 are abnormal. So can diagnose and cure or prevent earliest the cancers.

Conclusion: This proposal is worth to be further researched and applied to clinical practice and prevention. And tries to propose a new molecular biology research method.

Is it Necessary for Surgical Excision in Benign Papillary Lesions Initially Diagnosed at Core Needle Biopsy?

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Purpose: The aim of our study is to propose the management guidance of benign papillary lesions initially diagnosed at core needle biopsy.

Methods: Between January 2003 and January 2006, 76 lesions were identified to benign papillary lesions at initial core needle biopsy (n=68) or vacuum biopsy device (n=8) and who subsequently underwent surgical excision in all cases. There were 67 simple benign papilloma and 9 atypical papilloma. The final pathology of 76 papillary lesions were classified as one of the following: intraductal papilloma (n=56), papillomatosis (n=5), atypical papilloma (n=9), ductal carcinoma in situ (n=1), or papillary carcinoma (n=5).

Results: Six of 68 benign papillary lesions initially diagnosed at core biopsy were confirmed malignant papillary neoplasm. Consequently, the false negative rate of core biopsy was 8.8%. Three of 8 atypical papillomas were confirmed papillary cancer in final pathology. False negative rate of core biopsy for atypical papilloma was 37.5%. However, The false negative rate of core biopsy for atypical papillary lesions initially diagnosed at vacuum biopsy were 0%. Malignant papillary lesions were located more periphery than benign lesions (p=0.005) and larger than benign papillary lesions in tumor size (>1.5 cm) (p=0.017).

Conclusion: The results of this study demonstrate that malignant papillary lesions are larger in tumor size and located more periphery than benign lesion. The false negative rate of vacuum biopsy was 0%. Consequently, vacuum biopsy is very accurate method for identification of papillary lesion. In atypical papilloma, false negative rate was very high (37.5%). It is concluded that atypical papilloma at initial core biopsy or clinically peripheral located and large sized papilloma (>1.5 cm) need surgical excision.

Immunohistochemical Distinction of MUC1 in Ductal Intraepithelial Neoplasia (DIN1a, Flat Epithelial Atypia) and Breast Carcinoma

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Purpose: MUC1 is a large transmembrane glycoprotein, and high expression of MUC1 is associated with aggressive tumors. Therefore, MUC1 antigen is used as a marker to monitor disease progression in breast cancer patients. The aim of this study was to evaluate the differential patterns of MUC1 expression in different histological types of breast carcinoma and ductal intraepithelial neoplasia.

Methods: 22 normal breast, 7 intraductal hyperplasia (IDH), 33 ductal intraepithelial neoplasia (DIN1a) and 307 malignant lesions were selected and immunostained with MUC1. The patterns of reaction were classified as intraluminal border (ILB), cytoplasmic, intercellular membrane (ICM), intranuclear or mixed staining.

Results: All the normal breast showed weak cytoplasmic staining. All the IDH showed moderate cytoplasmic and ILB staining. Of the 33 DIN1a lesions, MUC1 was observed in 12 (36.3%) with weak cytoplasmic staining, 21 (63.6%) with moderate cytoplasmic and ILB staining. Of the 307 malignant lesions, only 2 (0.8%) showed negative; MUC1 was observed in 4 (1.3%), with ILB; 8 (2.6%) with weak cytoplasmic, 16 (5.2%) with weak cytoplasmic and intranuclear, 168 (54.7%) with moderate cytoplasmic and ILB, and 109 (35.5%) with strong cytoplasmic and ICM staining.

Conclusion: These data suggest the expression of MUC1 was different in normal breast, IDH, DIN1a and malignant breast tumors, and was significantly correlated with the histological tumor types. MUC1 could be a useful marker in early carcinomas and ductal hyperplasia.

Excision of Benign Breast Tumor by an Ultrasound-guided Mammotome Biopsy Device

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Purpose: Percutaneous vacuum-assisted breast biopsy (Mammotome, Fa. Ethicon Endo-Surgery) is now commonly performed as the initial approach to diagnose and treat benign breast lesions. It can obviate the need for surgery in women with benign lesions and often lead to a one-stage surgical procedure when malignant lesions are diagnosed. The purpose of study was to report the outcome of the Mammotome biopsy.

Methods: We performed 902 cases of Mammotome biopsy (total 474 patients) to confirm the diagnosis and to excise the lesion between January 2003 and December 2006 at Chosun University Hospital. Among these cases, 453 cases (total 261 patients) with radiographically suspected benign lesions, below BI-RADS category 4, were followed up for more than 6 months and we analyzed clinical and pathologic results of these 453 cases, retrospectively. Ultrasonographic follow-up examinations were performed and no malignant tumor or atypical ductal hyperplasia was included.

Results: The mean age was 42 (range: 17-76) years. The average size of lesion was 1.12 cm (range: 0.20-5.0). In BI-RADS category, there were 280 (62.0%) C2, 28 (6.0%) C3 and 145 (32.0%) C4 lesions. Histology revealed 294 cases (65.7%) of fibrocystic change, 100 (22.3%) fibroadenomas, 8 (1.5%) intraductal papillomas, 14 cases (2.9%) of sclerosing adenosis, 16 cases (3.3%) of ductal epithelial hyperplasia, 8 cases (1.5%) of fat necrosis, 3 cases (0.7%) of gynecomastia, 10 cases (2.1%) of chronic inflammation. 382 lesions (84.3%) were completely removed, 62 cases (13.7%) of residual lesion and 9 cases (2.0%) of postoperative scar were reported.

Conclusion: Mammotome biopsy is a effective diagnostic and therapeutic management of benign breast lesions with minimal-invasiveness and minimizes postoperative complications, such as parenchymal distortions or scars.

Evaluation of Interphase FISH on Aspirate Specimen for the Detection of HER2 Gene Amplification

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Purpose: This study was performed to assess the performance of interphase HER2 FISH on aspirate specimen (PCNA) comparing on formalin fixed paraffin embedded (FFPE) tissue specimen.

Methods: Fine needle aspirate specimens were collected before scheduled surgery. Cells were split onto two slides after being pelleted and fixed. One slide was processed to perform HER2 FISH and the other for Giemsa staining. We also performed HER2 FISH on the matched FFPE tissue slides and compared the results with PCNA FISH and FFPE tissue immunohistochemistry (IHC). FISH results were interpreted according to new criteria recommended by ASCO/CAP.

Results: Twenty six out of 31 (84.0%) specimens showed concordant results among PCNA FISH, tissue FISH and tissue IHC. One specimen out of 31 (3.2%) showed positive HER2 FISH and IHC on FFPE tissue but negative on PCNA FISH. Since we observed no cancer cells on the corresponding Giemsa-stained slide to the specimen which showed discordance, it should be excluded by FISH interpretation criteria. Discrepancies observed in 2 specimens out of 31 were caused by new equivocal criteria. Two specimens showed concordant results between FISH on PCNA and tissue, only discordant to IHC.

Conclusion: Our data suggested that PCNA specimens can be successfully used for interphase FISH to detect HER2 gene amplification.

Efficacy of Ultrasound-Guided Mammotome Biopsy for Breast Tumor

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Purpose: Core needle biopsy (CNB) is the routine method of preoperative pathological diagnosis for breast tumors in our institution. However, we have often experienced the cases that have discordance between the radiological and the pathological diagnosis or that histological diagnosis indicated benign lesion despite the stump cytology of the biopsy specimen showed positive. We have been undergone a mammotome biopsy (MMTB) under ultrasonography guiding for such a cases.

Methods: Thirty-five women who have received MMTB between February 2005 to October 2006 were reviewed on the bases of their medical records. The median age of the patients was 48.0 years old (range 19-75) and the median tumor size was 1.4 cm (range 0.5-4.2). Eighteen patients had non-palpable tumors. The indications of MMTB were following, 7 cases showed atypical cell clusters in the CNB specimens, 10 cases had suspicious stump cytology of CNB specimens, 15 cases diagnosed benign lesion despite the imaging diagnosis seemed to be malignant lesion, and 3 miscellaneous cases.

Results: Eight cases out of 35 were malignant including 4cases of DCIS, 2 cases of invasive ductal carcinoma, a case of malignant phyllodes tumor and a case of malignant lymphoma. No malignancy was appeared among 27 cases who had diagnosed as benign lesion by MMTB.

Conclusion: Ultrasonography guided MMTB is a useful method for diagnosis of breast tumors, which is difficult to make a definitive diagnosis by routine CNB.

Sexual Function in Breast Cancer Patients

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Purpose: We evaluated the sexual function in patients with different adjuvant treatment modalities for breast cancer.

Methods: Assessment tool was the female sexual function index (FSFI), a questionnaire evaluating six domains (desire, arousal, lubrication, orgasm, satisfaction and pain). In this longitudinal study patients answered the questionnaire prior to surgery (visit 1), and 3 months (visit 2) and 6 months (visit 3) after surgery while adjuvant treatment. 85 patients were included in the study and answered the first questionnaire. Nine patients, who had no sexual activity at visit 1, were excluded from the study. 36 patients did not answer the questionnaires at visit 2 or visit 3. 40 patients answered the questionnaires at visit 1, 2 and 3 and were eligible for evaluation. 10 patients (25%) received adjuvant chemotherapy (FEC x 6), 15 patients (37.5%) received antihormone therapy with tamoxifen and 15 patients (37.5%) received ovarian suppression with goserelin and antihormone therapy with tamoxifen.

Results: The FSFI total score decreased from 24.46 at visit 1 to 13.68 at visit 2 ($p < 0.001$) and 18.34 at visit 3 ($p = 0.001$) in the chemotherapy group, but was nearly constant with 20.89 at visit 1, 19.97 at visit 2 ($p = 0.53$) and 20.43 at visit 3 ($p = 0.75$) in the Tamoxifen group and slightly decreased from 29.96 at visit 1 to 28.30 at visit 2 ($p = 0.26$) and 27.69 at visit 3 ($p = 0.13$) in the GNRH/Tam group.

Conclusion: Female sexual functioning is reduced in patients receiving chemotherapy compared to patients receiving Tamoxifen only or GnRH analogues plus Tamoxifen

Care Using Breast Prostheses for Post-Mastectomy Breast Cancer Patients First Report: Effects Immediately after Care Implementation

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Purpose: To elucidate the effects of care for post-mastectomy patients provided by nurses with expertise in breast prostheses.

Methods: Care using prostheses was provided to post-mastectomy breast cancer patients by trained nurses who had acquired skills in lectures using models and were currently participating as trainees in an accredited breast cancer nursing program. The status of prosthesis prior to care and the effects of prosthesis immediately and three months after care were investigated. In the present report, the effects of care were analyzed based on the responses of subjects immediately after care. Subjects were recruited with the cooperation of patient groups, and cooperation in the study was requested based on ethical considerations. Contents of care using prostheses: Following assessment of previous methods of prosthesis and its physical, mental, and social aspects, a silicone prosthetic pad and special brassiere were proposed to subjects.

Results: Immediately after care, the 10 subjects reported that they were satisfied with the fit, excited about dressing up, and had found items that fit. The effects of care included enhanced femininity and satisfaction in life (Tables 1-3).

Conclusion: Care using prostheses that fit patients provided by nurses with expertise is useful for enhancing patient satisfaction.

Table 1 Background of subjects

Age	48-77 years (mean, 61.2 years)
Years since surgery	4-20 years (mean, 9.3 years)
Type of surgery	Modified radical mastectomy (n=9) Radical mastectomy (n=1)

Table 2 Previous methods of prosthesis

Use of breast prosthesis	Yes (n=8) No (n=2)
Method of obtaining information regarding prosthesis (multiple answers)	Patient groups (n=8) Brochures at hospitals (n=5) Exhibits by manufacturers of prosthetic products (n=4)
Method of prosthesis (multiple answers)	Sponge pad (n=5) Silicone pad (n=4) Handmade pad (n=4)
Frequency of use of prosthetic pad	Everyday (n=6) Only when going out (n=2)

n=10

Fig 1. Background of subjects

Table 3 Effects of prosthesis care

1) Satisfaction with fit:	<ul style="list-style-type: none"> · I was not really interested at first, but when I actually tried it on, it fit my body well and I felt as though I had my breast back · I realized that even slight differences in size can change the fit completely, etc.
2) Excitement about dressing up	<ul style="list-style-type: none"> · The fitting went well, and I'm excited about being able to dress up · I was excited when I found out that bras come in many different designs · I was very happy to find out that I could wear bras that match the current fashion, etc.
3) Finding items that fit	<ul style="list-style-type: none"> · I am satisfied because the nurse carefully selected items that fit and provided care kindly and politely · I really appreciated how the nurse considered and offered items for various breast shapes and found a wonderful pad for me, etc.

Fig 2. Effects of prosthesis care

Care Using Breast Prostheses for Post-Mastectomy Breast Cancer Patientssecond Report: Effects Three Months after Care Implementation

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Purpose: To elucidate the effects of care for post-mastectomy patients provided by nurses with expertise in breast prostheses.

Methods: Care using prostheses was provided to post-mastectomy breast cancer patients by trained nurses who had acquired skills in lectures using models and were currently participating as trainees in an accredited breast cancer nursing program. The status of prosthesis prior to care and the effects of prosthesis (five items graded on a four-point scale and free response) immediately and three months after care were investigated. In the present report, changes in the feelings of patients regarding prostheses were analyzed by focusing on the effects three months after care. Subjects were recruited with the cooperation of patient groups, and cooperation in the study was requested based on ethical considerations. Contents of care using prostheses: Following assessment of previous methods of prosthesis and its physical, mental, and social aspects, a silicone prosthetic pad and special brassiere were proposed to subjects.

Results: No significant differences in responses on a four-point scale were observed between immediately and three months after care for the scores. However, on free response, patients reported they obtained a more suitable method of prosthesis, and continued using the prosthesis and expressed satisfaction three months after care (Tables 1-3).

Conclusion: Care using prostheses that fit patients provided by nurses with expertise is useful for enhancing patient satisfaction.

Table 1 Background of subjects

Age	48-77 years (mean, 61.2 years)
Years since surgery	4-20 years (mean, 9.3 years)
Type of surgery	Modified radical mastectomy (n=9) Radical mastectomy (n=1)
Previous use of prosthesis	Yes (n=8) No (n=2)

n=10

Table 2 Concerns in daily life

	Immediately after care (mean value*)	Three months after care (mean value*)
I am worried about breast prosthesis	2.3	1.8
I am reluctant to go out	1.1	1.1
I am worried about people looking at me	1.4	1.4
I feel less feminine	1.6	1.5
I lack confidence in myself	1.3	1.4

* Mean values were calculated for each item as follows:
Not really, 1; Slightly, 2; Sometimes, 3; Always, 4.

Fig 1. Background of subjects, Concerns in daily life

Table 3 Changes in the patients' feelings

<p>1) I obtained a more suitable prosthesis</p> <ul style="list-style-type: none"> • I am satisfied because the item fits me better than the pad I had previously been using • I use it to match the TPO, etc. <p>2) I became more confident</p> <ul style="list-style-type: none"> • I became more confident and cheerful because I could wear T-shirts in the summer • I became more energetic and confident <p>3) I started dressing up more</p> <ul style="list-style-type: none"> • I felt like dressing up a little before going out, even for casual outings, etc.
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Fig 2. Changes in the patients' feelings

Care Using Breast Prostheses for Elderly Breast Cancer Patients Who Have Undergone Mastectomy

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Purpose: To elucidate the effects of care for post-mastectomy patients provided by nurses with expertise in breast prostheses.

Methods: Care using prostheses was provided to elderly breast cancer patients who have undergone mastectomy by nurses who had acquired skills in lectures using models and were currently participating in an accredited breast cancer nursing program. The status of prosthesis prior to care and the effects of prosthesis immediately and three months after care were investigated. In the present report, changes in the feelings of patients and care that promoted these changes were analyzed. Subjects were recruited with the cooperation of patient groups, and cooperation in the study was requested based on ethical considerations.

Results: Although the two subjects had respectively obtained information from patient groups and corporations in the past, they had not used prostheses (“I did not put much effort”, “It was on my mind but I did not take any action”), nor felt the need to use them in daily life considering their age. Following care, the subjects realized the “benefits of prostheses” in their lives, and continued to use the prosthesis and reported expansion of their lifestyles as well as satisfaction after care (Tables 1-3).

Conclusion: Care using prostheses that fit patients provided by nurses with expertise is useful for enhancing patient satisfaction.

Table 1 Background of subjects

	Subject A	Subject B
Age	70s	70s
Years since surgery	20 years	5 years
Type of surgery	Modified radical mastectomy (bilateral)	Modified radical mastectomy

Table 2 Status of prosthesis prior to care and effects immediately and three months after care

	Subject A	Subject B
Method of obtaining information regarding prosthesis	Explanation from nurse Exhibit by manufacturer of prosthetic products	Patient group
Status of prosthesis prior to care	I did not put much effort into prostheses because I am old	It was on my mind, but I did not use prostheses or take any action
Effects immediately after care	It felt great when I tried it on I am excited about dressing up	I am happy I got the opportunity for a fitting I am happy because the nurse selected a pad that fits my body
Effects three months after care	I use it only when I go out I would have liked to have started using this earlier	I use it everyday I felt like dressing up and going out I felt more energetic and confident

Fig 1. Background of subjects, Effects of prosthesis care

Table 3 Changes in the patients' feelings and care that promoted these changes

Changes in the patients' feelings	<ul style="list-style-type: none"> • I began to realize the "benefits of prostheses" in my life • I felt like dressing up and going out, and my lifestyle became broader • I was satisfied because the prosthetic pad fits my body
Nursing care that promoted changes in the patients' feelings	<ul style="list-style-type: none"> • Consideration of the size, shape, and weight of pads according to the patient's preferences • A gradual approach based on the patient's feelings, in which fitting was performed after asking the patient to confirm the feel of the pad with her hands • Sufficient assessment of the condition of the patient's chest wall, and consideration of the orientation of the pad and shape of the bra such that they fit the patient's body • Respect for the "comfort of the patients themselves", rather than forcing opinions as nurses

Fig 2. Care that promoted changes in the patients

Quality of Life with the Breast Cancer Patients and Their Spouses across the Treatment Phases in Republic of Korea

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Purpose: The aims of this study were to assess similarities and differences between patients with breast cancer and their spouses across the treatment phases and to investigate the relationships between the patients' and spouses' quality of life.

Methods: The convenience sample consisted of 45 women and their husbands in operation phase, 13 women and their husbands in adjuvant treatment phase, and 31 women and their husbands in recovery phase. Participants completed a questionnaire which contained a demographic questionnaire, and Quality of life questionnaire (Ferrell's QOL-BC and QOL-Family version). Descriptive statistics, t-test, and ANOVA tests were used to analyze the data. Differences were found across phases of treatment on subscales and total QOL scores, including those representing perceived physical well being, psychological well being, social well being, spiritual well being, and total QOL.

Results: Psychological wellbeing score of breast cancer patients were significant differences across the treatment phases ($F=3.83$, $p=0.025$). However, no significant differences were found across the treatment phases in husbands. There was a significant relationship between total QOL and subscales of breast cancer patients and their spouses across the treatment phases.

Conclusion: Health care professionals need to recognize similarities and differences between women and their husbands to better meet the needs of patients and their husbands with a breast cancer diagnosis and treatment. Future studies need to consider nursing care intervention for breast patients and their spouses across the treatment phases.

Informational Needs of Korean Women with Breast Cancer: Cross-Cultural Adaptation of the Toronto Informational Needs Questionnaire of Breast Cancer

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Purpose: The purpose of the study was to adopt an instrument suitable for assessment of the informational needs of Korean women with breast cancer and to identify informational needs of them.

Methods: A quantitative approach was used in which data were collected by means of a survey based on the instrument, the Toronto Informational Needs Questionnaire of Breast Cancer (TINQ-BC) under development, and the data were analyzed to assess the psychometric properties of the instrument.

Results: Three of 52 items of the TINQ-BC were found to be ineffective at measuring informational needs of Korean women with breast cancer. The revised scale, Korean Informational Needs Questionnaire-Breast Cancer (KINQ-BC), consisted of 49 items. The informational needs of Korean women with breast cancer were high with a mean total KINQ-BC score of 207.44 (35.13 SD) ranged 109 to 260. When the total KINQ-BC score of the sample (n=164) was standardized according to the questionnaire's 5-point scale, it was 4.23. This is between 4 (very important) and 5 (extremely important) indicating high levels of informational need. Korean women diagnosed with stage 3 breast cancer had the highest informational needs (4.61, standardized mean), while women whose stage was unknown had the lowest ones (3.66, standardized mean).

Conclusion: The TINQ-BC which was developed and tested in Canada was adapted and successfully utilized in this study in Korea, indicating that it has the potential to assess the informational needs of women with breast cancer on an international basis.

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The Lived Experience of Illness and Treatment in Hospital among Patients with Breast Cancer

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Purpose: The purpose of this retrospective qualitative study was to describe how breast cancer patients experience their illness and treatment. The life-threatening potential of cancer and the perception of potential or actual suffering for treatment do impact patients' progress and daily living.

Methods: The participants for this study were 8 women, who were over the age of 30 having the treatments of surgery, chemotherapy and radiotherapy because of breast cancer. Data were collected by using in-depth interviews and observations, analyzed using a hermeneutic phenomenological approach outlined by van Manen.

Results: The essential themes fit into the context of the 4 existential grounds of corporeality, temporality, spatiality and relationality. The themes were 'being doubtful about the cancer diagnosis', 'a long interlude between result and operation after checkup', 'alternating hope and despair due to medical staffs' slight manner', 'endurance of long painful treatment period', 'body in fragile condition', 'the fear of uncertainty', 'uncomfortable but secure hospital room' 'support of family and fellow for recovery'.

Conclusion: The findings indicate that patients with breast cancer need continuity of support and information that is patient-centered and holistic as treatment progresses. Therefore it is necessary for nurses to understand the patients' situation during treatment and their desire for a return to normal living. This study can assist nurses caring breast cancer patients to give more sensitive and appropriate care. Further research is needed on nursing intervention that could help breast cancer patients cope with and find the meaning in their suffering.

Effects of Fighting Spirit Promoting Program on Fighting Spirit and Self Care Behavior in Patients with Breast Cancer

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Purpose: The purpose of this study was to develop a fighting spirit promoting program for cancer patients and to test its effect on patients' fighting spirit, helplessness, anxiety, and self-care behaviors.

Methods: Three types of approaches to enhance fighting-spirit were developed: 1) a 15-minute long Web-based flash contents for vicarious experiences; 2) a 20-minute long education program & a 10-minute long telephone call coaching for verbal persuasion; and 3) a booklet for symptom management and fighting spirit promoting strategies. The evaluation was done by a nonequivalent control group pretest-posttest design. Study subjects were 17 breast cancer patients undergoing chemotherapy for experimental group and 27 for control group. The experimental group were received a 4-week intervention, 30-50 minutes a day weekly, and measured the variables at baseline, and 8weeks later. Fighting spirit and helplessness were measured by MAC (mental Adjustment to Cancer) and anxiety was measured by Hospital Anxiety and Depression scale. Self-care behaviors Scale developed by Oh et al., (1997) was used. Data was analyzed by Chi-square test, Mann Whitney U test, Wilcoxon rank sum test using SAS 9.13 program.

Results: The experimental group revealed significantly more fighting spirit ($z = -3.84$, $p = 0.000$), more self-care behaviors ($z = -4.27$, $p = 0.000$), and No difference, however, was found in anxiety ($z = -1.84$, $p = 0.077$) and helplessness ($z = -1.84$, $p = 0.0003$) between the two groups.

Conclusion: These results suggested positive effects of a hope-spirituality and self efficacy intervention program on fighting spirit. Self-care behaviors increased mainly through an increase in fighting spirit.

The Characteristics of Treatment-Related Quality of Life in Early Phase after Breast Cancer Treatments

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Purpose: The aim of the study is to investigate the characteristics of treatment-related QoL in early phase after breast cancer treatments through regular follow-up.

Methods: Five hundred seven women who had the surgical treatment for breast cancer were evaluated at regular interval of 3 months from pre-operative to 6 months after surgery. The reviews of types of treatments were recorded. Patients fulfilled the self administered questionnaire: Disability of the Arm, Shoulder and Hand (DASH), Brief Pain Inventory (BPI), Beck Depression Inventory (BDI) and European Organization for Research Treatment of Cancer (EORTC) Quality of Life Questionnaire-C30 and BR23.

Results: Patients who had total mastectomy complained of more deteriorated upper limb functions than patients who had lumpectomy did, and also tended to be more depressive at postoperative 6 months. Patients who had SLNBx were not statistically differ from patients who had ALND in overall QoL. Rather, patients with SLNBx showed lower QoL in several specific items (emotional function, breast and arm symptoms) at post-operative 6 months. Chemotherapy had a significant influence on upper limb function, QoL and depression at postoperative 3 months. Radiotherapy lowered the QoL related to future perspective and breast symptoms at postoperative 6 months.

Conclusion: Treatment-related QoL has various features according to types of surgery and adjuvant treatments. Especially, it is noteworthy that the QoL of patients with SLNBx had undistinguished QoL compared to patients with ALND, rather showed lower QoL regarding the emotional functions and pain or discomfort.

The Development and Evaluation of Web-Based Flash Content for Fighting Spirit Promotion in Patients with Cancer

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Purpose: The purpose of this study was to develop a Web-based flash content for fighting spirit promotion and to test its effect on cancer patients' fighting spirit.

Methods: The 15-minute long Web-based flash content was developed using the following 5 process: analysis, planning, development, program operation and evaluation stages and utilized the multiple edition and revision processes from December 2005 to August 2006. The evaluation was done by one group pretest-posttest design. Study subjects were 17 cancer patients undergoing chemotherapy. The group were received a 2-week intervention, a day weekly, and measured the variables at baseline, 4 weeks later. The study was performed from August 2006 to February 2007 at a cancer center in Korea. Fighting spirit was measured by Mini-MAC (Mental Adjustment to Cancer). Data was analyzed by descriptive statistics and paired t-test using SAS 9.13 program.

Results: On the Web-based flash content, there are 4 menu bars that consisted of cancer diagnosis, symptom management, stress management, and cancer survivorship. The study group revealed significantly more fighting spirit than pre-test ($t = -58.24$, $p = 0.0001$).

Conclusion: This Web-based flash content can be utilized in psychosocial interventions for promoting fighting spirit in patients with breast cancer.

The Chemotherapy-Induced Long-term Amenorrhea in Premenopausal Women with Breast Cancer

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Purpose: Long-term survivors of young patients with breast cancer are at risk for menopause. The aim of this study is to determine the incidence and the predictors of chemotherapy-induced long-term amenorrhea in premenopausal women with breast cancer.

Methods: Eighty premenopausal patients with breast cancer were treated with adjuvant chemotherapy from 1999 to 2004 were included. The chemotherapeutic agents were one of the following regimens: cyclophosphamide, methotrexate, and 5-fluorouracil (CMF x 6); doxorubicin and cyclophosphamide (AC x 6); AC followed by paclitaxel (AC-T, AC x 4 and T x 4).

Results: The mean age of patients at diagnosis was 40.8 years. Sixty patients (75.0%) developed long-term amenorrhea: 82.9% in CMF; 60.0% in AC; and 70.8% in AC-T. The older patients were at higher risk of menopause (≥ 40 years 80.8% vs. < 40 years 64.3%). There was a statistically significant association between age and the development of menopause in CMF but not in AC, AC-T regimens. In ≥ 40 years old patients, menopause was related to the types of chemotherapeutic regimens (93.1% in CMF; 44.4% in AC; and 78.6% in AC-T), but not in < 40 years old patients. Parity, age of menarche, BMI, tumor size, and nodal status were not related to the menopause.

Conclusion: The development of chemotherapy-induced menopause was associated with older patients at higher risk and was higher in CMF group than AC or AC-T group. The incidence of menopause according to adjuvant chemotherapeutic regimens was different between < 40 years and ≥ 40 years old patients.

The Development and Longitudinal Change of Upper Limb Dysfunctions in Breast Cancer Patients

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Purpose: Longitudinal changes of upper limb dysfunctions through regular follow up were understudied. This study aimed to investigate upper limb dysfunctions for breast cancer patients before, 3 and 6 months after surgery.

Methods: We enrolled 507 breast cancer patients of two tertiary hospitals from July, 2006 to March, 2007. Eighty-two patients completed follow-up at regular intervals of 3 months from pre-operative to 6 months after surgery. Subjective symptoms, range of motion (ROM), impingement signs, pain and upper limb disability questionnaire — Disability of the Arm, Shoulder and Hand and Brief Pain Inventory — were evaluated at baseline, 3 (T1) and 6 months (T2) after surgery.

Results: Most declines in upper limb function were occurred for 3 months after surgery. Arm swelling, arm pain, shoulder pain, arm or shoulder tightness, dull sense and arm weakness were mainly encountered in T1, then persisted to T2. However, stiffness and tingling were more frequently developed at T2 than T1. Limitation of ROM, positive impingement signs, pain intensity and upper limb disabilities were increased at T1 than baseline, and those findings showed no significant changes at T2. Patients with mastectomy had more upper limb problems than patents with breast conserving surgery. No significant differences in upper limb functions were found between sentinel node biopsy and axillary lymph node dissections.

Conclusion: Upper limb dysfunctions were mostly developed for 3 months and persisted to 6 months after surgery. These results highlight the necessity of early rehabilitation for upper-limb functions, especially in patients with total mastectomy.

Examining Mediation Effect of Perceived Physical Suffering between Perceived Negative Treatment Effect and Hope in the Cancer Patients just after Surgery for Cure

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Purpose: The purpose of this study is to examine whether perceived physical suffering could function as a mediation variable between perceived negative treatment effect and hope.

Methods: In descriptive and correlational design, survey of perceived negative treatment effect (PNTE) and perceived physical suffering (PPS) with responses on visual analog scales, and hope with responses on Kim and Lee Hope scale consists of 39 items ($\alpha=0.956$ at this study) were administered to a convenience sample of 130 cancer patients (breast cancer 45, stomach cancer 49, and etc. / 54 male and 76 female / mean age: 56.3 ± 12.4 / mean POD: 7.1 ± 4.5) just after surgery for cure. The data were analyzed using the three regression equations derived from Baron and Kenny's three equations: simple regression equation for the effect of PNTE on PPS, simple regression equation for the effect of PNTE on hope, and multiple regression equation of the effect of PNTE and PS on hope.

Results: PNTE explained the variance of PPs with 6.7% ($p<0.01$) and the variance of hope with 25.3% ($p=0.000$), and PNTE and PPS explained hope with 26.6%. Therefore, the basic conditions needed for testing the mediation effect of PPS between PNTE and hope were satisfied. When the effect of PPS on hope was controlled, the coefficient for correlation of PNTE to hope was decreased from -0.503 ($p=0.000$) to -0.463 ($p=0.000$).

Conclusion: The mediation effect of PPS between PNTE and hope were verified. Based on the result, hope inspiring or promoting intervention for the cancer patients just after surgery could be done.

The Relationship between Hope and Depression in Women with Breast Cancer Patients

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Purpose: This study was to identify the relationship between hope and depression in women patients suffering from breast cancer.

Methods: The subjects of this study were 106 breast cancer patients who were under treatment at out patients department and admitted at Pusan University hospital in Busan. The data were collected by using structured questionnaire from February 18, 2007 to April 14, 2007. Instrument used for this study were Hope scale developed by Nowotny's (1989) and amended by Choi (1990), Self-rating Depression Scale was developed by Zung (1965) and amended by Kwon (1994). The reliability of this study were each Cronbach's $\alpha=0.801$ and 0.709 . The collected data was analyzed using t-test, Scheffe's test, ANOVA and Pearson Correlation Coefficients.

Results: 1. The mean of hope was 84.43 ± 11.07 (range of scale: 27 to 116, 51 min, and 111 max). The mean of depression was 31.95 ± 7.51 (range of scale: 15 to 60, 17 min, and 60 max). 2. There were significant difference in hope according to religion ($F=3.985$, $p=0.010$), religious faith ($F=8.635$, $p=0.000$), regional effect on life ($F=4.213$, $p=0.004$), positive attitude during the treatment ($F=5.798$, $p=0.003$). In depression according to the level of religious faith ($F=8.635$, $p=0.000$), regional effect on life ($F=4.213$, $p=0.004$), and positive attitude during the treatment ($F=3.319$, $p=0.040$). 3. There was a significant negative correlation between hope and depression ($r=-0.542$, $p=0.000$).

Conclusion: Hope of patients with breast cancer was related to depression. And the hope where the relation variables are examined closely, it could be will be used to reduce depression of the patients with breast cancer as strategy of nursing intervention.

The Relationship between Spiritual Health and Depression in Women with Breast Cancer Patients

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Purpose: The purpose of this study was to find out the relationship between spiritual health and depression in women patients with breast cancer.

Methods: The subjects of this study were 145 breast cancer patients who were breast cancer diagnosis at several general hospital in B city. The data was collected by using structured questionnaire from January 20, 2007 to May 30, 2007. The Instruments used for this study included Highfield's Spiritual Health Inventory and amended by Lee and Kim (1998), the Self-Rating Depression Scale by Zung (1965) and by Kwon (1994). The reliability of this study were each Cronbach's $\alpha=0.801$ and 0.709 . The collected data was analyzed using t-test, Scheffe's test, ANOVA and Pearson Correlation Coefficients.

Results: 1. Spiritual health score was over moderate (107.07 ± 14.61 ; range of scale: 75 to 142), depression score was normal level (45.58 ± 6.99 ; range of scale: 26 to 65). 2. There were significant difference in spiritual health according to financial state ($F=6.675$, $p=0.002$), fatigue ($F=8.386$, $p=0.000$), the effect of religion on personal life ($F=5.746$, $p=0.004$), In depression according to financial state ($F=3.734$, $p=0.026$). 3. Spiritual health in women patients with breast cancer indicated a significant negative correlation to depression ($r=-0.306$, $p=0.000$).

Conclusion: It is needed strategies for intervention of spiritual health to reduce the depression in women patients with breast cancer. The significant several characteristics of related to spiritual health & depression should consider in psychospiritual nursing intervention of breast cancer patients.

Factors of Occurrence of Amenorrhea and Climacteric Symptoms in Breast Cancer Patients Who Underwent Chemotherapy

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Purpose: To investigate the pattern of menstrual changes and factors of occurrence of amenorrhea and the severity of climacteric symptoms in breast cancer patients who underwent chemotherapy.

Methods: Women were recruited from S hospital located in Seoul, and included if who were diagnosed with breast cancer without metastasis or recurrence; had surgery, followed by chemotherapy; and had their period at the time of breast surgery. A total of 99 women aged 31 thru 55 years agreed to participate and filled out a structured questionnaire including the Functional Assessment Cancer Therapy-Breast plus Endocrine Symptom when they visited the clinic for a follow-up.

Results: Amenorrhea occurred in 88 women within the average of 2 months since they had started chemotherapy, and the period was resumed later only in 11 women. About 98% of women aged over 40 experienced their period stopped, thus age was an apparent factor related to the occurrence of amenorrhea ($\text{Exp(B)}=0.76$, $p<0.05$). Presence of chronic disease ($\text{Beta}=0.25$, $p<0.05$) and body weight change ($\text{Beta}=0.30$, $p<0.01$) were significant factors influencing the severity of climacteric symptoms.

Conclusion: Nurses need to have clinical evidences of menstrual changes due to cancer treatment in women with breast cancer. Information about premature menopause and climacteric symptoms should be provided according to women's health conditions so that they cope better during their survivorship.

Family Needs Satisfaction and State Anxiety according to the Method of Offering Information during Cancer Surgery

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Purpose: This study was conducted to compare according to the two kinds of methods of offering information during cancer surgery on the family needs satisfaction and state anxiety.

Methods: This research is quasi-experimental study of a total 80 patients with half of them experimental group. Experimental group was assigned to be served text-information by cellular-phone and control group was direct message by nurses during peri-operative time. Peri-operative family needs and anxiety were measured and analyzed by χ^2 -test and t-test.

Results: There were no significant difference of the level of peri-operative family needs satisfaction and the level of state anxiety between the direct peri-operative information group and the text message group ($p>0.05$).

Conclusion: Based upon the above finding, it seemed that the nursing intervention with cellular phone short message is as effective as direct peri-operative information in reducing the level of state anxiety and in increasing of the level of nursing needs satisfaction of the patients' families.

Post Operative Arm Morbidity in Breast Cancer Patients within 2 Years after Surgery

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Purpose: Most breast cancer patients after surgery have suffered the arm morbidity. This study is to describe the severity of post operative arm morbidity in breast cancer patients within 2 years after surgery.

Methods: A cross-sectional, descriptive design was used for this study and the data were collected using the self-reported questionnaire including FACT-G, 5 subscales of FACT-B+4 and the medical records. The subjects were 183 breast cancer patients between 1month and 24months after surgery.

Results: 1. Arm morbidity was experienced 86.9% (159/183) patients. This included 72.8% (133/183) patients experienced the pain, 42.9% (78/183) patients experienced the poor ROM, 69.6% (127/183) patients experienced the numbness, 55.4% (101/183) patients experienced the stiffness, 41.3% (75/183) patients experienced the swelling. 2. 19.7% (36/183) patients reported the severity of arm morbidity was “quite a bit” or “very much”. This included 21.7% (40/183) patients experienced the pain, 17.4% (32/183) patients experienced the poor ROM, 21.2% (39/183) patients experienced the numbness, 12.5% (23/183) patients experienced the stiffness, 10.8% (20/183) patients experienced the swelling. 3. BMI ($p=0.026$), sentinel lymph node biopsy ($p=0.027$), radiotherapy with axillary ($p=0.032$), chemotherapy ($p=0.019$) were significantly related to the severity of arm morbidity. 4. For 2 years after surgery, the severity of the arm morbidity was not different with time significantly ($F=0.150$, $p=0.962$).

Conclusion: Arm morbidity was most common in breast cancer patients after surgery but seem to be experienced very hard for only some patients (19.7%). In future, it must be studied with careful consideration to the relative factors of arm morbidity.

(mean range: 0-4)

Symptom	Not at all (%)	A little bit (%)	somewhat (%)	Quite a bit (%)	Very much (%)	Mean (SD)
Pain	50 (27.2)	73 (39.7)	20 (10.9)	33 (17.9)	7 (3.8)	1.80 (0.99)
Poor ROM	105 (57.1)	32 (17.4)	14 (7.6)	23 (12.5)	9 (4.9)	2.11 (1.08)
Numbness	56 (30.4)	63 (34.2)	25 (13.6)	34 (18.5)	5 (2.7)	1.85 (0.95)
Stiffness	82 (44.6)	50 (27.2)	28 (15.2)	18 (9.8)	5 (2.7)	1.78 (0.91)
Swelling	108 (58.7)	43 (23.4)	12 (6.5)	17 (9.2)	3 (1.6)	1.73 (0.95)

Fig 1. The severity of arm morbidity.

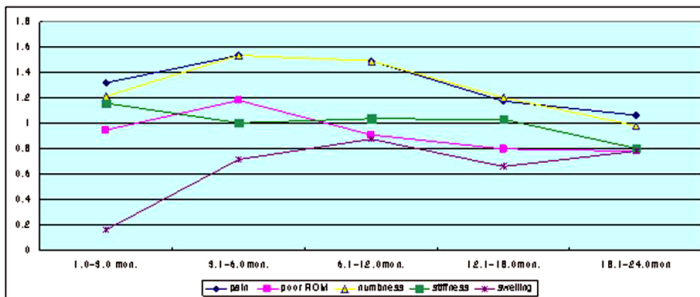


Fig 2. The severity of arm morbidity according to time

Quality of Life after Breast Cancer Surgery: An Asian Perspective

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Purpose: Breast cancer is one of the most common cancers amongst women in Asia. Singapore has one of the highest incidences of breast cancer in this region. The quality of life after breast cancer surgery has been widely studied in the West, but there is limited data on Asian women. Our aim is to do a pilot study on the quality of life in Asian women after breast cancer surgery in Changi General Hospital.

Methods: Due to cultural and religious differences between Asian and Western population, we customized a questionnaire to address common local concerns. We focused on physical, emotional, functional and social well-being of the patient. We compared the findings with the patient's demographics and tumour characteristics.

Results: Between March.

Conclusion: Most of the women coped well after breast cancer surgery. Body image issues are more important in younger women and those who had mastectomy. Older women generally coped better.

Efficacy of Comprehensive Group Rehabilitation for Women with Early Breast Cancer in South Korea

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Purpose: The purpose of this study was to evaluate the effects of a comprehensive group rehabilitation program on the range of motion of the shoulder joint, psychosocial adjustment, and the quality of life for early breast cancer patients.

Methods: Fifty-five women with early breast cancer were assigned to an intervention group or a control group. The eligibility criteria included patients with: histologically confirmed early stage (stages I, II) breast cancer with no evidence of recurrent or progressive disease; a timeframe within 2 years after the mastectomy; the completion of chemotherapy and/or radiotherapy with or without current hormone therapy use; no mental disease or systemic disease. The intervention was provided three times per week for 10 weeks. The intervention consisted of psychology-based education, exercise (group and home-based), and peer support group activity.

Results: The results showed an increased range of motion of the shoulder joint, and psychosocial adjustment and quality of life were shown to be significantly higher in the intervention group than in the control group.

Conclusion: The rehabilitation program comprised psychology-based education, exercise, and peer support group activity to promote recovery of the affected shoulder joint range of motion, alleviate physical symptoms, and improve psychosocial adjustment and quality of life for early breast cancer patients in South Korea.

Study of the Depression and the Quality of Life in Patients with Breast Cancer

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Purpose: This study was designed to investigate not only the prevalence of the depression in patients with breast cancer but also the correlation between the depression and the quality of life in patients with breast cancer.

Methods: Forty-one patients with breast cancer were selected, who had visited the department of General surgery of the Wonkwang University Hospital with a diagnosis of breast cancer regularly during the period November, 2005~May, 2006. All subjects were evaluated for the depression and the quality of life. The measure included Beck Depression Inventory (BDI), Short-Form 36 Health Survey-Korean version (SF-36).

Results: The prevalence of depression in patients with breast cancer is 36.4%. Compared to the patient group with radiation therapy, the patients without radiation therapy had the significantly higher mean scores on SF-36. But the mean scores on SF-36 was not influenced by menopause, tumor size, cancer stage, surgery type, chemotherapy and hormone therapy. Compared to patient group without depression, the patient with depression had the significantly lower mean scores on six subscales in SF-36 [Physical function ($p<0.01$), Role-physical ($p<0.001$), General health ($p<0.05$), Social function ($p<0.001$), Role-emotional ($p<0.001$)]. But there are no significant difference between two groups in the Vitality and Bodily pain.

Conclusion: It is possible that about a half of the patients with breast cancer undergo depression and their depression influence on quality of life. These findings suggest that some patient treated for breast cancer need to have psychiatric evaluation and management on depression.

The Quality of Life, Depression, Stress Hormone, Immunity and Heart Rate Variability in Patients with Breast Cancer

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³*Department of Psychiatry, College of Medicine, Wonkwang University, Korea*

Purpose: This study was designed to investigate not only the prevalence of the depression in patients with breast cancer but also the correlation between the depression and the quality of life in patients with breast cancer.

Methods: Forty-one patients with breast cancer were selected, who had visited the department of General surgery of the Wonkwang University Hospital with a diagnosis of breast cancer regularly during the period November, 2005~May, 2006. All subjects were evaluated for the depression and the quality of life. The measure included Beck Depression Inventory (BDI), Short-Form 36 Health Survey-Korean version (SF-36).

Results: 1) The prevalence of depression in patients with breast cancer was 36.4%.

2) There were positive correlations between depression or/and anxiety and somatic symptoms or/and pain. In addition, there were negative correlations between somatic symptoms and the social support and the quality of life as well as between pain and anxiety and the quality of life.

3) There was positive correlation between Physical Stress Index (PSI) of HRV and somatic symptom, and negative correlation PSI and quality of life. There were negative correlations between Total Power (TP) or Low Frequency (LF) and somatic symptoms, and positive correlations between TP or LF and quality of life.

4) There were significant difference in results of HRV between patients with breast cancer and healthy control.

Conclusion: It is possible that about a half of the patients with breast cancer undergo depression and their depression influence on quality of life. These findings suggest that some patient treated for breast cancer need to have psychiatric evaluation and management on depression.

Relationships among Body Image, Self-Esteem and Health Promotion Behavior in Mastectomy Patients

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Purpose: To fine out the relationships among body image, self-esteem and health promotion behavior in mastectomy patients.

Methods: Data were obtained by self-reported questionnaires from 218 patients undergone mastectomy from Sep. 1 to Oct. 15, 2005. And data were analyzed using SPSS/PC WIN 12.0. For the statistical analysis of the data, frequency and percentage, mean and standard deviation, t-test, ANOVA and Sheffe's test and Pearson's correlation coefficient were used.

Results: The mean scores of the body image, self-esteem and health promotion behavior of the subjects were 41.41 (range of scale: 17 to 68), 22.22 (10 to 40), and 130.45 (50 to 200) respectively. There were significant differences with the score of body image by the work type, a number of child, and participation with self help group program. There were significant differences with the score of self-esteem by the type of religion, work type, post operation period and participation with self help group program. There were significant differences with the score of the health promotion behavior by the type of religion, economic state, level of education, operation site, family history, and hope of breast reconstruction. Relationship between body image and self-esteem showed strong positive correlation ($r=0.631$), the relationship between body image and health promotion behavior showed slightly positive correlation ($r=0.257$), and the relationship between self-esteem and health promotion behavior showed moderate positive correlation ($r=0.431$).

Conclusion: For the increasement of the health promotion behavior, it is needed to improve body image and self-esteem in mastectomy patients, and to encourage to participate with self help group program in mastectomy patients.

Comparison of Fatigue and Depression in Breast Cancer Survivors

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Purpose: We performed this study to compare the correlates of fatigue with those of depression and to identify relevance of fatigue and depression to health-related quality of life (HRQOL) in disease-free breast cancer survivors.

Methods: A total of 1,933 breast cancer survivors recruited from five large hospitals in Korea completed a mailed survey, including the Brief Fatigue Inventory, Beck Depression Inventory, European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, and QLQ-BR23. With the framework including socio-demographic, clinical, and symptom characteristics, multivariate logistic regression models were used to identify factors associated with fatigue and depression.

Results: Among breast cancer survivors, 66.1% reported moderate to severe fatigue and 24.9% reported moderate to severe depression. Overall correlates of fatigue and depression differed, except for insomnia, which correlated with both. Fatigue was significantly associated with younger age and having a job, gastrointestinal disease, dyspnea, insomnia, arm symptoms, being upset by hair loss, and depression. On the other hands, depression was significantly associated with lower income, having a musculoskeletal disease, insomnia, appetite loss, constipation, financial difficulties, systemic therapy side effects, and fatigue. Neither condition was associated with treatment-related clinical factors. Both fatigue and depression were inversely related to survivors' HRQOL, depression to a greater extent. However, the patterns of differences in HRQOL according to prevalence of fatigue or depression were similar.

Conclusion: Our study provides insights that will enable new approaches to intervention in cases of fatigue and depression in breast cancer survivors.

The Effects of Long-Term Combined Exercise on Functional Fitness and BMD in Breast Cancer Survivors

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Purpose: This study was designed for the patients who wanted to improve their body functions and BMD (Body Mineral Density). In the study, we effectively developed the long-term combined exercise with a gradual increase in intensity and examined its effect on functional fitness and BMD in breast cancer survivors.

Methods: The subjects of this study were 40 to 60-year-old married women (n=24) who finished their treatments 6 months to 1 year ago and consumed 1,840-1,900 kcal/day. The exercise that they had was composed of HATA-Yoga, elastic-band and gym-ball exercise program. Six of the 24 women who were diagnosed as osteoporosis (T-score range -3.4 to -5.6) participated in the exercise program with osteoporosis drug (alendronate 70 mg per week plus 1,500 mg of calcium and 400 I.U. of vitamin D per day). The combined exercise program was designed 40-60 minutes/day and three times/week for a total of 48 weeks. The collected data was analyzed by the SPSS 12.0 version. The effectiveness of the multicomponent intervention was analyzed using descriptive (means, SDs, ranges, percentages) and comparative (repeated one-way ANOVA and posthoc Tukey, Wilcoxon signed rank test) analyses.

Results: Twelve months after, the participants had a significant increase in reach-ups, grip strength sit-ups test and FM of functional fitness. In BMD, the exercise group (n=18) had no change, while the exercise group with osteoporosis drug (n=6) had significant improvement.

Conclusion: The study showed that HATA-Yoga, elastic-band, gym-ball exercise program had the positive impact on functional fitness and delay BMD in breast cancer survivors. Especially, the exercise group with osteoporosis drug had significant improvement in BMD.

Table 1. Characteristics of the sample at baseline(N=24)

	M(SD)
Age(yrs)	50.7(4.9)
Height(cm)	157.3(5.3)
Body weight(kg)	57.2(5.7)
BMI(kg/m ²)	23.0(2.4)
SBP(mmHg)	121(10.9)
DBP(mmHg)	77.1(9.3)
Pulse rate(times)	74.7(7.2)
	n(%)
History of osteoporosis	
yes	6(25)
no	18(75)
Stage breast cancer	
0	2(8.3)
1	12(50.0)
2	10(41.7)
Surgery method	
Breast conservation	15(62.5)
Mastectomy	9(37.5)
Menopause	
yes	14(58.3)
no	10(41.7)

Fig 1. Characteristic of the subjects

Table 2. Change in functional fitness

Items	Baseline M(SD)	16weeks M(SD)	32weeks M(SD)	48weeks M(SD)	F-value	P-value	Posthoc
Reach-ups(cm)	17.0(5.2)	19.0(5.3)	19.1(5.3)	19.9(4.7)	12.93	.002	1<2, 1<3, 1<4
Grip st.(R)(kg)	22.6(4.4)	23.6(4.7)	24.3(3.3)	25.1(3.5)	7.55	.012	1<3, 1<4
Grip st.(L)(kg)	20.6(4.4)	20.9(5.7)	23.4(3.2)	23.1(3.4)	11.43	.003	1<3, 1<4, 2<4
Back scratch(R)(cm)	1.4(11.7)	0.4(9.4)	-0.6(9.1)	-0.2(8.9)	.937	.34	
Back scratch(L)(cm)	-3.4(11.8)	-1.9(10.5)	-0.8(9.6)	-2.0(9.7)	2.539	.13	1<3
Sit-ups(times)	17.4(7.4)	20.5(8.8)	21.8(10.6)	21.8(10.4)	12.754	.002	1<2, 1<3, 1<4
One-foot balance(sec)	18.6(13.8)	23.2(18.6)	27.3(19.0)	17.8(16.1)	.025	.88	1<3
FM(kg)	18.6(13.8)	18.1(4.4)	18.3(3.9)	17.6(4.0)	471.470	.000	1>2, 3>4
LBM(kg)	20.7(1.9)	20.7(1.7)	20.6(1.5)	20.5(1.8)	3.282	.08	
WHR(ratio)	0.89(0.05)	0.89(0.05)	0.88(0.04)	0.91(0.05)	.111	.74	1>3

Values are mean±standard deviation. * : p<.05, ** : p<.0.1, *** : p<.001

Table 3. Change in BMD of the exercise group

Ex.G. (N=18)	Site	Pre	Post	Z	P
		M(SD)	M(SD)		
	L1	134.3(19.4)	130.4(17.86)	-0.707	.099
	L2	129.9(20.7)	129.5(17.1)	-0.157	.480
	L3	126.3(21.5)	125.9(14.9)	-0.079	.875
	T12	133.7(25.2)	127.7(29.5)	-1.650	.937
	T-s.	-2.2(0.8)	-2.2(0.6)	-.634	.526

Table 4. Change in BMD of the exercise group with osteoporosis drug

Ex. G. (N=6)	Site	Pre	Post	Z	P
		M(SD)	M(SD)		
	L1	68.6(24.7)	78.3(27.0)	-2.207	.027
	L2	61.1(35.1)	79.2(28.9)	-1.363	.173
	L3	71.1(19.8)	78.9(24.0)	-1.782	.075
	T12	77.4(27.5)	89.3(26.5)	-2.201	.028
	T-s.	-4.6(0.9)	-4.1(0.9)	-2.207	.027

Values are mean±standard deviation, * : p<.05

Fig 2. Results

The Effects of Korean Hand Acupuncture on Nausea, Vomiting, Fatigue and Depression of Breast Cancer Patients Undergoing Chemotherapy

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¹*Department of Nursing, College of Medicine, Inje University, Korea*

Purpose: The purpose of this study was to identify the effects of Korean hand acupuncture nausea, vomiting, fatigue and depression in breast cancer patients undergoing chemotherapy.

Methods: The research was a quasi-experimental study using a non-equivalent pre-post design and was conducted from March 5 to May 20, 2007. The subjects consisted of 32 patients with 17 in experimental group and 15 in control group. A pretest and 2 posttest were conducted to measure nausea, vomiting, fatigue and depression. For the experimental group, aluminum bead was placed on the Korean hand acupuncture point on both hands for 12 hours each time. This treatment was given six times by a researcher and 2 research assistants. The research instruments included the Index of Nausea and Vomiting by Rhodes and McDaniel (1999), Revised Piper Fatigue Scale by Piper et al (1998), and Beck Depression Inventory-Korean Version. The collected data were analyzed by repeated measures ANOVA using SPSS WIN 12.0 program.

Results: There was statistically significant decrease in nausea, vomiting and fatigue in the experimental group compared to the control group over two different times. But there was no statistically significant difference in depression in the experimental group compared to the control group over two different times.

Conclusion: The Korean hand acupuncture was effective on the nausea, vomiting and fatigue in breast cancer patients receiving chemotherapy in this study. Therefore, the Korean hand acupuncture can be usefully utilized as nursing intervention for the breast cancer patients undergoing chemotherapy in the field of cancer nursing.

Multidisciplinary Approach in Palliation of Aggressive Breast Cancer

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Purpose: Palliative Care should begin at cancer diagnosis (Fig 1). This case study illustrates the multidisciplinary approach, the difficulty in differentiating radical and palliative intents, and effectiveness of radiotherapy (RT) in fungating mass palliation.

Methods: Summary: 49 years-old Malay woman with T4aN1M0 Grade 3 Infiltrative ductal carcinoma of left breast and negative ER/PR/CerbB2 status (5/2006). She underwent neoadjuvant Docetaxel/Ketoconazole for 4 cycles (clinical trial), left total mastectomy and level 3 axillary clearance (15/8/2006). There was partial response (PR), clear resection and 20/21 positive lymph nodes with focal/extensive extranodal extension. In 9/2006, she had small left chest wall (CW) recurrence, treated with Adiamycin/cyclophosphamide (2 cycles) then RT to left CW/SCF/Axilla (50 Gy/25#) and posterior CW lesions (35 Gy/14#), but tumour spread to right breast. She was depressed. Gemcitabine/carboplatin (4 cycles) yielded PR. Pain score of 8/10 in right breast was helped by Morphine, Tramadol, Amitriptyline, 45 Gy/18# to right breast (Fig 2), daily dressing and lymphoedema physiotherapy.

Results: Three lines of chemotherapy gave PR, but RT achieved right breast pain score of 2/10, good tumour shrinkage and haemostasis. However, she died of further lung metastasis on 7/7/2007.

Conclusion: Multidisciplinary team (surgical/medical/radiation oncologists, palliation physician, psychiatrist, nurses, physiotherapist, social workers, counselor) helped her symptoms (breast pain, neuropathic pain, oedema, bleeding, depression) and improved her quality of life. RT (35-50 Gy) is effective for fungating tumour though no standard palliative dose fractionations exist.

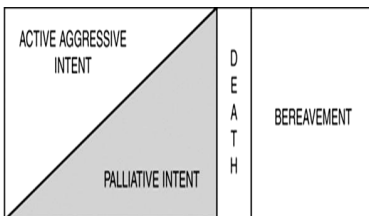


Fig 1. Shifting paradigm in anticancer treatment intent



Fig 2. Tumour spread to right breast after Left CW RT

Quality of Life of the Terminal Cancer Patients Receiving Home Care Nursing

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Purpose: The purpose was to investigate the level of QOL of the terminal cancer patients at home and to identify influencing factors on QOL.

Methods: Subjects consisted of 72 terminal cancer patients receiving home care nursing for more than 2 weeks in 6 general hospitals in Seoul. Data were collected by self-reporting questionnaire on QOL, pain, physical functioning, and symptom experience from Feb, 2006 to Dec, 2006. QOL was measured with questionnaire developed for terminal cancer patients by Yoon. Worst, average, and least pain during the last 24 hours were measured with 0-10 NRS. In addition, physical functioning and symptom experience were measured. Data were analyzed by t-test, one way ANOVA, Pearson correlation coefficients, and multiple regression using SPSS Win 14.0.

Results: Mean score of QOL was 98.6 (230 in total). In subcategories of QOL, the score of family & socio-financial domain was highest, and spiritual, psychological, and physical symptom domain were high in the order. Except the level of family coping general characteristics and disease related variables did not show significant difference in QOL. In the groups of higher family coping QOL was higher and QOL showed negative correlation with pain, physical functioning and symptom experiences. Least pain, physical functioning, and level of family coping explained QOL in 26.7%.

Conclusion: Pain, physical functioning, symptom experience, and family coping were related with QOL and the least pain, physical functioning and level of family coping were important factors influencing on QOL of terminal cancer patients. However, some other variables influencing the QOL need to be explored.

Patient-Physician Communication on the Complementary and Alternative Medicine (CAM) Usage in Radiotherapy (RT) Patients: A Singaporean Experience

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Purpose: Good patient-physician communication is vital in optimal cancer care. Many cancer patients use CAM therapies without disclosing to their oncologists. We conducted a pilot study to find out a) the reasons for patients' non-disclosure of CAM usage; b) the patients' perceptions of RT doctors' responses; c) Asian cancer patients' needs, besides answering other CAM questions.

Methods: A survey on CAM practices was conducted among 65 RT patients in TCI@NUH from December 2004 to January 2005, using modified MD Anderson Questionnaire (English/Chinese). Two trained research assistants obtained consent from the patients and interviewed them. The frequency of patients' reasons and doctors' responses was calculated.

Results: All patients were Asians (86% Chinese, 6% Malay, 6% Indian/others) and 41.5% had breast cancer. Main reasons for non-disclosure were patients' uncertainty about doctors' care (reason 1: doctors never ask, 73.9%) and doctors' responses (reasons 2-6) [Fig 1]. Seventy-three percent of RT doctors discouraged the CAM usage from responses 1, 2 and 4: encouraged patients to stop (33%); being neutral (33%); warned about the risk (7%) [Fig 2].

Conclusion: This study highlights the need for open patient-physician communication. Because of cultural differences and respect for doctors, Asian patients tend to ask less questions during consultation. It is good for doctors to initiate discussion on CAM usage during or after RT and offer evidence-based advice, acknowledging uncertainty in CAM-RT interactions. Further studies are still needed.

REASONS	NUMBER (%)
1. The doctor never asked about other therapies	34 (73.9%)
2. Patients were unsure if CAM therapies were beneficial	26 (43.5%)
3. The doctors would not understand	5 (10.9%)
4. It was not important for the doctor to know about it	5 (10.9%)
5. The doctor would discourage or disapprove	3 (6.5%)
6. The doctor might not continue as the provider	2 (4.3%)
7. Patients were confident about doctor's decisions	1 (2.2%)
8. Patients were confident about hospital therapies	1 (2.2%)
9. Patients planned to discuss with doctors later	1 (2.2%)
10. Going for spiritual healing	1 (2.2%)

Fig 1. Patients' reasons for non-disclosure of CAM usage

RT DOCTORS' RESPONSES	%
1. Encouraging patients to stop using CAM therapies	33
2. Being neutral about using CAM therapies	33
3. Encouraging me to continue using CAM therapies	20
4. Warning patients of the risks of using CAM therapies	7
5. Others	7

Fig 2. Responses of 15 RT doctors at TCI@NUH

Shared Decision-making in Treatment Decisions for Breast Cancer in Korea

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Purpose: We aimed to understand medical decision making in the context of shared decision-making. We investigated the relationship between shared decision-making and type of surgical treatment for women with breast cancer.

Methods: 1,927 of 4,439 eligible women who had undergone primary curative surgery for localized breast cancer from five hospitals in Korea between 1993 and 2002 responded to a survey questionnaire. A wide range of socio-demographic and clinical data, and self-reported decision-making information were obtained.

Results: Overall 69.6% of women received mastectomy. Most women reported they discussed on surgery (89.1%), radiotherapy (84.9%), and chemotherapy (90.4%). A fewer patients reported they discussed on hormone therapy (69.9%). Women who were older age (adjusted odds ratio [aOR], 1.86; 95% confidence interval [CI], 1.21 to 2.88) and unemployed at diagnosis (aOR, 1.21; 95%CI, 1.05 to 1.39), had advanced stage (aOR, 3.85; 95%CI, 3.20 to 4.63) and less income (aOR, 1.62; 95%CI, 1.41 to 1.41), discussed on chemotherapy (aOR, 3.18; 95%CI, 2.60 to 3.88) and hormone therapy (OR, 1.97; 95%CI, 1.68 to 2.32), not discussed on surgery (aOR, 1.21; 95%CI, 1.05 to 1.39) and radiotherapy (aOR, 1.20; 95%CI, 1.65 to 2.67), and whose opinion were not reflected in treatment decision (aOR, 1.38; 95%CI, 1.10 to 1.73) were more likely to receive mastectomy. Patient's involvement in decision-making was not a significant indicator of surgical treatment decision.

Conclusion: Our findings suggest shared decision-making process such as actual discussion on treatment and reflection of patient's own opinion were significant indicators of decision on surgical treatment in addition to sociodemographic and clinical characteristics.

‘Taste Good and Feel Good’ Support Group

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Purpose: Support groups for cancer patients are an essential part of the recovery and healing process. Most cancer support groups are directed towards Caucasian Americans and are unsuitable to many Asian American women due to cultural differences. Cooking is an important aspect of Asian culture, so cooking classes could be an excellent platform for cancer support. They offer the dual purpose of providing a safe, comfortable environment and excellent nutrition that could contribute to the health of cancer patients. A model for a cooking cancer support group is presented.

Methods: Weekly Korean cooking classes. 6 breast cancer patients and 4 family members participated as the chef provided step by step instruction.

Results: The formal quantitative research surveys are not a culturally competent method for assessing the success of this program for monolingual, Korean women with breast cancer. For this reason, we conducted informal interviews and discussions with the participants at the end of the ten week class series. There was not any measurement to determine the reduction in depression levels, however, all the participants developed friendships and reduced their isolation by coming to the cooking class every week.

Conclusion: The traditional Western style support group is not culturally sensitive to many timid and reserved immigrants. Cooking is a very effective way of getting Korean cancer patients out of isolation and reducing their anxiety and depression. It reflects a culturally competent approach and also provides valuable nutritional benefits.

Effect of a Multidisciplinary Educational Program in Breast Cancer Patients

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Purpose: The aim of the study was to compare and evaluate a multidisciplinary educational program with traditional intervention after breast cancer surgery in terms of knowledge about their disease and compliance with therapeutic regimen.

Methods: A nonequivalent control group pretest-posttest design was used. Forty-six consecutively selected women with newly diagnosed, classified as stage I or stage II, participated in either a multidisciplinary educational program (n=25), or traditional intervention (n=21) from October to December, 2006. The multidisciplinary educational program (MEP) was led by a physician, a specialist nurse in oncology, and a dietitian, composed of 2 sessions for a week. Dependent variables were measured at baseline and one-week follow up. The collected data was analyzed by using SAS 8.0 statistical program.

Results: The mean age of the sample was 48 years. At baseline the groups had similar characteristics. Patients in the MEP reported significantly more level of knowledge about their disease and compliance with therapeutic regimen.

Conclusion: The MEP improves level of knowledge about their disease and compliance with therapeutic regimen in breast cancer patients. However, there is a need for further research in relation to timing of the multidisciplinary educational program, i.e. when to introduce multidisciplinary approaches after operation, and the cost benefit from such educational interventions. In addition, the experience from this MEP could be used in the future when developing web-based educational, program.

Predictors of Participation in Support Groups among Women with Breast Cancer

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Purpose: This study examined what characteristics and variables predict to participation in support group for women with breast cancer.

Methods: 282 women with breast cancer from 4 hospitals located in Busan were included in the study. Data was measured on each participant from September 2006 to February 2007. It was collected using structured researcher-administered sheets and analyzed by descriptive statistics, t-test, chi-square test and logistic regression analysis.

Results: The clients reported medium levels of illness perception, anxiety and depression, stress coping, social support and self-efficacy. The 48.9% of women with breast cancer participated in support groups. Significant influencing factors on the participation in support groups were ‘operation time(+)’, ‘illness perception(+)’, ‘social support(-)’, and ‘self-efficacy(+)’ those variables explained 73.4%.

Conclusion: It is necessary to develop a strategy or promoting program for promotion of illness perception and self-efficacy of women with breast cancer. Thus it is essential to provide a participation to support group to women with breast cancer.

Quality of Life of Women with Breast Cancer in Delhi

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Purpose: During the last decade, survival rates for breast cancer have increased due to early detection and increased use of adjuvant therapy. Little is known about Quality of Life (QOL) of Indian women having breast cancer.

Methods: To study various domains of Quality of Life viz. physical, psychological, social and spiritual well being, of study subjects. Descriptive study in Lok Nayak Hospital in New Delhi. QOL in all 131 newly diagnosed breast cancer patients during the year 2006 was assessed by using validated standardized questionnaire (Version QOL-CS) for quality of life of breast cancer patients. All four domains of quality of life i.e. physical, psychological, social, and spiritual well being were studied. SPSS-pc software used and variables were compared by using analysis of variance (ANOVA) with respect to stage of cancer, age groups, and etc.

Results: Mean age of the patients was 47.5 years and the majority (62%) patients were in T4 stage. Patients were stratified in three age groups, (Younger than 40 years, 40-60 years, and older than 60 years). Most (53.4%) patients were in 40-60 years age group. Mean QOL subscores were 7.42 for physical well being, 5.08 for psychological well being, 5.70 for social well being, and 7.33 for spiritual well being.

Conclusion: Indian women with newly diagnosed breast cancer experienced poorer QOL related to psychological and social domains.

Evaluation of the Function and Contents of Web-Based Educational Program for Women with Breast Cancer in Korea

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Purpose: The purpose of this study was to evaluate the effectiveness of web-based breast cancer educational program which consists of special features such as flash animations and online counseling as well as 7 different categories of information on breast cancer.

Methods: The effectiveness of the program was analyzed in terms of its function and contents. A total of 147 women with breast cancer who visited the website for at least 30 minutes with minimum 3 times participated to the survey.

Results: In the satisfaction evaluation of web-based educational program, usefulness of information, system efficiency, adequacy of information and system convenience all received positive evaluation and showed even distribution of 49.14 (± 6.05) points out of 64 points total. In the usefulness evaluation, the subcategories had following scores from the highest to the lowest; understanding of breast cancer was 3.34 (± 0.51), life after treatments (3.21 ± 0.58), early detection and examination (3.20 ± 0.60), chemotherapy and hormonal therapy (3.18 ± 0.55), related factors and prevention (3.16 ± 0.59), treatments (3.13 ± 0.53), and diagnosis (3.02 ± 0.56). Factors affecting the satisfaction of the program were age, religion, income, stage of disease at diagnosis, source of health information, duration of internet usage, and whether the patient performs breast self-examination. Factors that affect the usefulness of the program were religion, period since diagnosis, source of health information, frequency of internet usage, recurrence of breast cancer, and family history.

Conclusion: Although the program was evaluated as somewhat useful and satisfactory, it should be improved more by providing in-depth and cutting edge breast health information especially for women with high educational backgrounds and income.

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Effects of Aerobic Exercise Using a Flex-Band on the Cardio-Pulmonary Function and Physical Flexibility of Breast Cancer Women Undergoing Radiation Therapy

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Purpose: This study examined the effect of aerobic exercise using a flex-band on the cardio-pulmonary function and flexibility in women undergoing radiation therapy after mastectomy.

Methods: The twenty six women who had received mastectomy and were undergoing radiation therapy were conveniently recruited from a University Hospital in Gwangju, South Korea. Study design was a non-equivalent control group pre- and post-test. The experimental group (n=15) performed aerobic exercise with 60% to 80% intensity of maximal heart rate for 25 minutes, 3 times a week for 6 weeks. The measurement tools were Ergocycle, POLAR Sport Tester, goniometer (American Medical Association Mode), and sit and reach tester. Data were analyzed using Mann-Whitney U test of SPSS program.

Results: The systolic blood pressure of the exercise group was significantly lower than the control group (p=0.008). The period till arrival THR and VO₂max in exercise group were significantly greater than control group (p<0.001; p=0.027) (Fig 1). The overall flexibility (ROM of the affected shoulder Joint, sit and reach, and back and reach) in exercise group was significantly greater than control group (p<0.01) (Fig 2).

Conclusion: Aerobic exercise using a flex-band can be a feasible exercise program that enhances cardio-pulmonary function and flexibility for women with mastectomy. Further studies are needed to examine the effects of early exercise intervention within post-operative 10 days and to repeat the same study design in a larger sample.

Cardio-pulmonary Function	Pre-test		Post-test		Mean Diff. (Mean Rank)	z-value (p)
	M ± SD (Mean Rank)	M ± SD (Mean Rank)	M ± SD (Mean Rank)	M ± SD (Mean Rank)		
SBP at Rest(mmHg)						
Experim. G. (n = 15)	112.00±13.20 (14.37)	100.13±10.57 (11.07)	-11.87±12.68 (16.70)			-2.852 (.008)
Control G. (n = 11)	108.18±14.71 (12.32)	109.09±12.21 (16.82)	0.91±8.31 (9.14)			
DBP at Rest(mmHg)						
Experim. G. (n = 15)	76.00±15.02 (15.00)	67.33± 7.99 (13.03)	-8.67±17.27 (15.07)			-1.262 (.207)
Control G. (n = 11)	69.09± 9.44 (11.45)	70.00±11.83 (14.14)	0.91±8.31 (11.36)			
Periods till THR (sec)						
Experim. G. (n = 15)	182.93±181.17 (13.50)	370.13±310.98 (17.53)	187.20±161.88 (9.00)			3.504 ($<.001$)
Control G. (n = 11)	135.45±67.61 (13.50)	120.00± 76.51 (8.00)	-15.45±80.29 (19.64)			
VO₂max (ml/min/kg)						
Experim. G. (n = 15)	16.87±2.30 (12.93)	17.01±2.24 (13.43)	0.14±0.33 (10.70)			-2.208 (.027)
Control G. (n = 11)	17.24±1.95 (14.27)	17.10±1.98 (13.59)	-0.14±0.12 (17.32)			

Fig 1. Cardio-pulmonary Function

Flexibility	Pre-test		Post-test		Mean Diff. (Mean Rank)	z-value (p)
	M ± SD (Mean Rank)	M ± SD (Mean Rank)	M ± SD (Mean Rank)	M ± SD (Mean Rank)		
Flexion-affected (180°)						
Experim. G. (n = 15)	152.80± 9.78 (12.17)	165.87±6.88 (16.17)	13.07±8.49 (8.60)			3.822 ($<.001$)
Control G. (n = 11)	156.27±15.23 (15.32)	156.00±14.94 (9.86)	-0.27±5.37 (20.18)			
Extension-affected(60°)						
Experim. G. (n = 15)	47.53± 9.77 (14.37)	51.87±6.68 (16.63)	4.33±6.51 (10.13)			2.645 (.008)
Control G. (n = 11)	46.18± 5.78 (12.32)	44.36±7.33 (9.23)	-1.82±5.25 (18.09)			
Ext. rotation-affected(90°)						
Experim. G. (n = 15)	85.20± 7.29 (15.57)	88.07±3.67 (17.73)	2.87±5.03 (9.47)			-3.493 ($<.001$)
Control G. (n = 11)	78.91± 8.95 (10.68)	75.73±9.93 (7.73)	-4.18±5.71 (19.00)			
Int. rotation-affected(70°)						
Experim. G. (n = 15)	61.67±20.29 (13.67)	73.00±17.05 (16.33)	11.33±10.51 (8.13)			4.187 ($<.001$)
Control G. (n = 11)	65.27±11.31 (13.27)	60.91±11.88 (9.64)	-4.36±8.77 (20.82)			
Sit & Reach (cm)						
Experim. G. (n = 15)	12.48±9.77 (14.27)	17.65±8.27 (16.13)	5.17±4.72 (8.67)			3.77 ($<.001$)
Control G. (n = 11)	10.91±8.55 (12.45)	10.80±8.68 (9.91)	-0.11±1.72 (20.09)			
Back & Reach (cm)						
Experim. G. (n = 15)	-8.61±14.01 (12.40)	-2.79±7.25 (13.37)	5.81±8.56 (10.13)			2.62 (.009)
Control G. (n = 11)	-3.67±8.64 (15.00)	-4.36±9.20 (13.68)	-0.69±3.25 (18.09)			

Fig 2. Physical Flexibility

Predictors of Quality of Life in Breast Cancer Survivors

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Purpose: This study was to identify predictors of quality of life in breast cancer survivors.

Methods: The data was collected from one hundred twenty two patients with breast cancer from November 1, 2006 to December 25, 2006 using a structured questionnaire after receiving study permission. Ferrell's Quality of life scale was used to assess quality of life. SPSS/WIN 12.0 was used for analyzing data.

Results: The mean age of the patients was 51 years. The mean elapsed time after operation was 38.03 (SD: 31.9) months. Quality of life mean score was 5.34 (SD: 1.36) points. Age, religion, pain, function of upper extremities, anxiety and perceived severity were significantly associated with QOL. In a regression analysis, anxiety, perceived severity, age and pain were significant predictors for QOL ($r^2=55.5$).

Conclusion: Physical and psychological factors were strong predictors of QOL. These results demonstrate the need for interventions to improve QOL in breast cancer survivors.

A Study on Behaviors for Preventing Recurrence and Quality of Life in Breast Cancer Survivor

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Purpose: This study was to get the basic data of the recurrence prevention behaviors for developing recurrence prevention program for a breast cancer survivors.

Methods: This descriptive study was conducted from November 1, 2006 to December 25, 2006 using a structured questionnaire. One hundred and twenty two women with breast cancer survivors were recruited using a convenient sampling method.

Results: The most frequent behavior for preventing recurrence of the breast cancer was dietary treatment (90.9%) and exercise (86.8%) was second order behavior. And the effectiveness was that 'very effective' was 82.8%. The degree of the quality of life of a breast cancer survivor was 5.34 points.

Conclusion: breast cancer survivors had various behaviors for preventing recurrence of breast cancer. Therefore, the nursing intervention for the breast cancer survivor will be focused systematic educational approach about behaviors for preventing recurrence to improve their quality of life.

Effects of a Staged Family Participation Program for Patients with Breast Cancer

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Purpose: The purpose of this study was to identify the effects of staged family participation program on physical and psychological status and quality of life for patients with breast cancer.

Methods: A quasi-experimental design was used. The subjects were 41 patients with breast cancer using convenient sampling method, 21 experimental group and 20 control group. The subjects of the experimental group participated in a staged family participating for patients with Breast cancer for four stages during 3 weeks. The staged family participation program of the study included supply of information on breast cancer, exercise, nutrition control and the breast cancer patients and their families participated. Physical and psychological outcomes were evaluated such as shoulder flexibility (Back & Reach test), grip strength (Bulb Dynamometer, Made in U.S.A.), pain (VAS), self- esteem (Jon, 1974), anxiety (Kim, Sin, 1978), and quality of life (Lee, 2000). Data was analyzed using the t-test of SPSS win 11.0 program.

Results: The scores of shoulder flexibility, grip strength, self-esteem, and quality of life increased significantly in the experimental group as compared to the control group. The scores of pain, and anxiety decreased significantly in the experimental group as compared to the control group.

Conclusion: The staged family participation program showed a large affirmative effect on physical, social, and psychological status and quality of life of breast cancer patients.

Study on the Effect of Exercise Program Based on Video on the Physical Functioning Recovery in Postmastectomy Patients

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Purpose: The purpose of this study was to demonstrate its feasibility that exercise program based on video gives confirmative influence for moderating patient's body condition, the range of motion of shoulder (flexion, extension & abduction), arm circumference of operative side and the intensity of pain.

Methods: This study was conducted with experimental design similar to the Non-Equivalent control group pre and post test 56 patients (28 respectively) in I and II stage, in which they had taken a breast surgery and were taking anti-cancer chemotherapy or a radiation treatment. The experimental group were provided with exercise program based on video for 24th week. Evaluation was performed 9 times in both the experimental and the control group respectively from April to December, 2006. The ROM of shoulder, arm circumference of operative side and the intensity of pain were measured.

Results: 1. The experimental group showed significant increase in the ROM of the shoulder.

2. In pain scale indicate large differences post op 16th week & 24th week in the experimental group.

Conclusion: This exercise program showed that the experimental group was improved the ROM of the shoulder and subsided pain. The case of postmastectomy is necessarily required the exercise for the upper part of the body. The exercise program utilized with multimedia mediums is expected to higher effect than learning through a book. Key words: Mastectomy, Exercise program based on video, ROM of the shoulder, Pain.

Quality of Life, Sexual Function, and Depression between Sex and Sexless Group

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Purpose: This study was to investigate the differences between quality of life, sexual function, and depression according to sexual activity among breast cancer survivors.

Methods: Subjects were breast cancer survivors who 48 sexless group and 55 sex group that participated at a self-help group in Gwangju, South Korea. Data were collected from June 9 to July 28, 2006. The questionnaires was composed of Quality of Life Index-Cancer Version (Q.L.I.-C) (Ferrans, 1990), self-rating depression scale (SDS) (Zung, 1965), and Female Sexual Function Index (FSFI) (Rosen et al., 2000). Data were analyzed using the SPSS Win 14.0 K+ for descriptive statistics, t-test, ANCOVA, and two-way ANOVA.

Results: There were not homogeneous in age, job, education level between two groups. There were analyzed to identify the differences of the research variables between two groups with controlling the covariates. The quality of life and sexual function in sex group were significantly higher than sexless group ($p < 0.001$). The depression in sex group were significantly lower than sexless group ($p < 0.001$) (Table 1-2).

Conclusion: These study indicates that sex professional are needed to counsel and intervene during the recovery period of breast cancer survivors.

Source	QOL					FSFI					Depression				
	SS	df	MS	F	p	SS	df	MS	F	p	SS	df	MS	F	p
Main effect : Sex group	32.041	1	32.041	15.772	(.001)	25688.266	1	25688.266	89.89	(.001)	1096.258	1	1096.258	19.379	(.001)
Covariate: Age	0.01	1	0.01	0.005	(.944)	0.657	1	0.657	0.002	(.962)	0.984	1	0.984	0.017	(.895)
Covariate: Education	8.302	1	8.302	4.086	(.046)	527.938	1	527.938	1.847	(.178)	44.925	1	44.925	0.794	(.375)
Error	197.063	97	2.032			25433.813	89	285.773			5487.361	97	56.571		
Corrected Total	253.647	100				63034.989	92				6917.485	100			

Fig 1. ANCOVA Table of QOL, FSFI, and Depression

Source	QOL					FSFI					Depression				
	SS	df	MS	F	p	SS	df	MS	F	p	SS	df	MS	F	p
Sex group	21.570	1	21.570	10.515	.002	22064.499	1	22064.499	75.735	.001	737.683	1	737.683	13.286	.001
Covariate: Job	4.920	1	4.920	2.398	.125	37.968	1	37.968	.130	.719	69.799	1	69.799	1.257	.265
Job * Sex group	.131	1	.131	.064	.801	66.888	1	66.888	.230	.633	16.611	1	16.611	.299	.586
Total	28243.829	101				222003.000	93				174166.000	101			
Corrected Total	253.647	100				63034.989	92				6917.485	100			

Fig 2. Two-way ANOVA of QOL, FSFI, and Depression

Genomic Copy Number Alterations as Predictive Markers of Systemic Recurrence in Breast Cancer

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Purpose: We tried to find novel predictive markers of systemic breast cancer recurrence by array comparative genomic hybridization (CGH).

Methods: We performed array CGH with 31 pairs of clinicohistologically well matched recurred/nonrecurred breast cancer tissues. We classified 3 groups such as R group (recurrence group, 31 samples), N group (nonrecurrence group, 31 samples), and A group (all group, 62 samples) for analysis. We selected those clones that hit the conditions of frequency criteria (more than 10%), consecutive clones (more than 2 clones), chi square test ($p < 0.05$), multiple comparison test (adjusted $p < 0.05$), and Kaplan-Meier test ($p < 0.05$).

Results: Eleven BAC clones in gain and 3 in loss were selected to be the candidate clones for predictive markers of systemic breast cancer recurrence. The most significant chromosomal alterations were found in the region of 5p15.33, 11q13.3, 15q26.3, 17q25.3, 18q23, 21q22.3 in gain, and 9p12, 11q24.1, 14q32.33 in loss. Especially, loss of 14q32.33 region was associated with good disease free survival ($p = 0.022$) and overall survival ($p = 0.019$). We selected 4 candidate genes in gain and 6 candidate genes in loss from 11 and 3 candidate clones, respectively.

Conclusion: Our array CGH analysis could detect novel candidate clones and genes for predictive markers of systemic breast cancer recurrence.

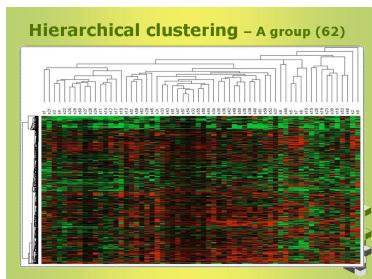


Fig 1. Hierarchical clustering - A group (62)

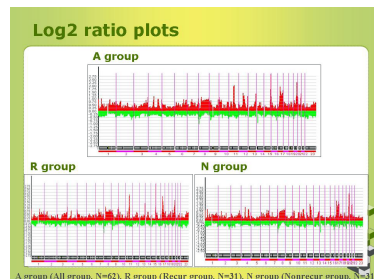


Fig 2. Log2 ratio plots

A Correlation between Breast Cancer Recurrence and Amplification of Cytokertin (CK) 20 in the Peripheral Blood and Bone Marrow

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Purpose: Most patients present stage I or II breast cancer and at least up to 30-40% of these patients will develop recurrent disease. These patients are considered as having disseminated cancer cells at the time of local treatment. Cytokeratin (CK) 20 is expressed in a majority of breast cancer. However, CK20 is not expressed in normal tissues or benign breast disease. The aim of study is to evaluate a correlation between the outcome of breast cancer and amplification of CK 20. And then, we found the role of CK amplification as prognostic predictor.

Methods: Between Jan 1999 and Aug 2003, the sample of blood and bone marrow was obtained from breast cancer who undertaken optimal surgical treatment at Korea University Hospital. We analysis 117 paired sample of blood and bone marrow using Real time PCR. A case who was revealed metastasis was excluded. A period of mean follow-up was 55 months.

Results: Each expression of CK 20 in the blood and bone marrow were shown in 31 (26.5%) cases and 48 (41%) cases, respectively. The expression of CK 20 in both was found in 19 (16.2%) cases. A significant difference of disease free survival between expression of CK20 in both and absent or only one sample was founded ($p=0.02$).

Conclusion: CK 20 is a useful predictor for the recurrence of breast cancer. Especially, the case with breast cancer was expressed in the both of blood and bone marrow.

Clinical Manifestation of Neck Node Metastases in Breast Cancer

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Purpose: Metastases to cervical lymph nodes do not exclusively derive from malignancies of the head and neck area. Metastases from various infraclavicular primary sites like breast cancer are known to occur in cervical lymph nodes. The aim of the present study was to analyse the clinical manifestation of lymph node metastases from breast cancer in the neck.

Methods: Among 2,522 patients with breast cancer operated in Cheil hospital from 1990 to 2004, 22 patients with neck node metastases were selected. A chart review was conducted to determine clinical manifestation retrospectively. The median age was 45.5 (range, 30 to 70 years). Mean follow up period from operation was 56.7 months and 17.1 months from diagnosis of neck node metastases. During follow up, 15 patients died with the mean survival duration of 20.7 months and 7 patients were alive.

Results: Eight patients had neck node metastases alone (36%), In 10 patients (45%), neck node metastases were detected first and then other site detected later. In one patient, neck node metastasis was identified after bone metastasis. Breast cancer-related distant metastases were diagnosed in eleven out of 22 patients. Metastases were located in the lung (6/11), bones (2/11), liver (2/11) and brain (1/11).

Conclusion: Neck node metastases can be detected easily by physical exam or ultrasound. In this study, ten cases of 11 with distant metastases were detected after diagnosis of neck node metastases. So diagnosis of neck node metastases can be useful to early detection of other distant metastases.

Clinical Relevance of PET/CT in Postoperative Follow-up of the Breast Cancer

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Purpose: Breast cancer is frequently characterized by increased 2-fluoro 2-deoxy D glucose uptake. We attempted clinical value of PET/CT in search of recurrent & meta-static breast cancer.

Methods: From March, 2004 to July 2007 postoperative PET/CT was performed at Saegyaero Hospital on 77 patients who underwent curative resection. Clinical outcomes were confirmed by clinicoradiologic course and biopsy. We surveyed concordance between PET/CT and Breast Ultrasound for locoregional recurrence.

Results: PET/CT results followed routine follow-up (59 cases, 76.62%), abnormal physical examination (5 cases, 6.49%), Equivocal bone scan (2 cases, 2.60%), Abnormal CT finding (2 cases, 2.60%), abnormal laboratory findings (6 cases, 7.79%), symptoms of patients (2 cases, 2.60%) and Abnormal Breast US (4 cases, 5.19%) Among the 77 PET/CT studies 34 were confirmed as having metastasis or recurrence, while 43 did not have metastasis and recurrence. 30 of the studies produced true positive results. 43 true negative. 13 false positive and 6 false negative. In the detection of postoperative metastases or recurrence of breast cancer the parameters for the use of PET/CT were 83.3% sensitivity, 76.7% specificity, 69.7% positive predictive value, 87.7% negative predictive value. On the basis of the lesion site, the accuracy of PET in the detection of bone (96%), lung (97.9%), liver (97.9%) metastases was superior to that of local recurrence (79.7%) or lymphnode metastasis (98%).

Conclusion: PET/CT may be useful in the evaluation of subgroup of patients for whom findings remain equivocal at the conventional postoperative follow-up methods for breast cancer, particularly in the detection of bone, lung and liver metastases. Combined PET/CT and breast Ultrasound imaging may be more beneficial for determination of locoregional recurrence.

Risk Prediction Model for Breast Cancer in Korean Women: National Health Insurance Corporation Study

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Purpose: The purpose of this study is to develop a risk prediction model for breast cancer in Korean women.

Methods: The data for this study came from the National Health Insurance Corporation Study (NHICS), Korean Central Cancer Registry and Korean Statistical Office. 162,231 women government employees and teachers with age between 30 and 80, and free of any cancer at the baseline were followed for upto 6 years. Two separate models using the Cox Proportional Hazard model were developed for women under age 50 and for those age 50 or more. The performance of the models was measured with respect to its discrimination and calibration ability.

Results: Two prediction equations were developed to predict breast cancer risk. C statistics for discrimination and a Hosmer-Lemehow type chi-square statistics for calibration of the models were calculated. For women under 50, age, body mass index, meat consumption, age at menarche, age at first childbirth were included in the model. C statistics was 0.633 (95% CI, 0.612-0.653) and the Hosmer-Lemehow type chi-square statistics was 6.807. For women age 50 or more, fasting glucose, exercise, age at menarche, and post-menopausal status were included in the model. The C statistics was 0.628 (95% CI, 0.520-0.719) and the Hosmer-Lemehow type chi-square statistics for calibration was 7.745.

Conclusion: This prediction model could be used for predicting individual risk of breast cancer development and providing useful information for the cancer prevention and early detection guidelines.

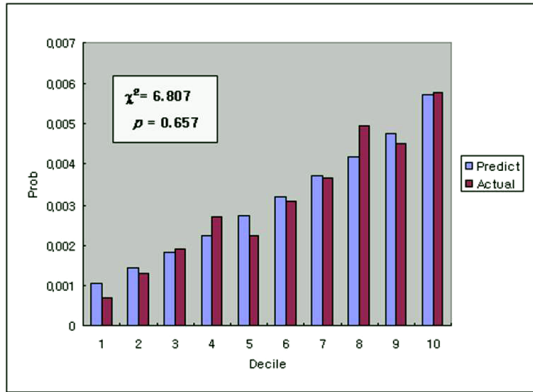


Fig 1. For women under age 50

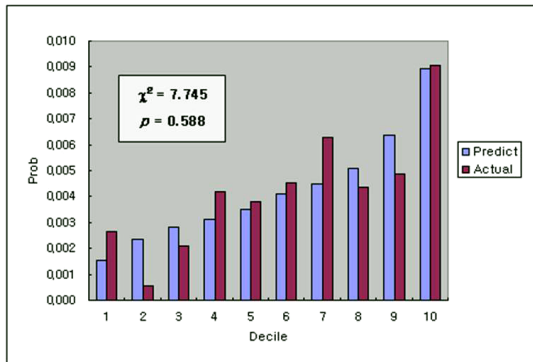


Fig 2. For women age 50 or more

Evaluation of Tau and ERCC1 as Predictive Markers for Breast Cancer Patients Treated with Paclitaxel and Cisplatin

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Purpose: The expression of tau, a microtubule associated protein, was shown to be associated with paclitaxel resistance in breast cancer. Excision repair cross-complementation group 1 (ERCC1) was related to cisplatin resistance in non-small-cell lung cancer. We planned to study the predictive and prognostic values of these two markers in breast cancer patients treated with combination chemotherapy of paclitaxel and cisplatin.

Methods: We retrieved patient data and archival tumors from 2 previous clinical trials using paclitaxel and cisplatin as first line chemotherapy for locally advanced breast cancer (LABC) or metastatic breast cancer (MBC). The expressions of tau and ERCC1 were examined by immunohistochemistry and correlated with overall response rate (ORR) and survival.

Results: A total of 46 patients (18 LABC and 28 MBC; median age, 53 years) with available archival tumors were enrolled. There were 2 complete responses (CR) and 24 partial responses (PR), and ORR of 59%. The expression of tau was significantly associated with lower response rate (44% vs. 77%, $p=0.02$). The expression of ERCC1 was not associated with ORR (58% vs. 62%, $p=0.81$). Intriguingly, higher response rate did not translate into longer progression-free survival (PFS) or overall survival (OS). On the contrary, there was a trend toward better PFS in patients with tau expression in univariate ($p=0.13$) and multivariate analyses ($p=0.15$).

Conclusion: The expression of tau, but not ERCC1, was a predictive marker for combination chemotherapy of paclitaxel and cisplatin in breast cancer patients.

Important Risk Factors of Distant Metastasis in Node-Negative Breast Cancer Patients

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Purpose: The risk categories of St. Gallen are widely used in postoperative adjuvant therapy. Our patients that used this category classification are High Risk 28.9%, Intermediate Risk 50.0%, and Low Risk 21.1%. The range of Intermediate Risk is also wide and many of lymph node-negative breast cancers are included. The importance is not clear although six risk factors were shown. However, in order to decide the adjuvant therapy, there is the necessity of clarifying the importance of their factors. To find more important risk factors of distant metastasis in node-negative breast cancers in our patients.

Methods: Axillary lymphnode-negative patients (pTx, pN0, pM0) which received the operation at the age of 65 or less from 1988 to 1998. The 29 patients which caused distant metastasis is all. But 120 patients which caused no distant metastasis was extracted at random which arranged time. The multi-variable analysis examined about Hormone Receptor Negative, Diameter of Tumor >2 cm, Histological Grade: 2 or 3, 35 or less years old, HER2 positive, and Ly >2+.

Results: 35 or less years old, HER2 positive, Histological Grade: 2 or 3 are more important risk factors for distant recurrence.

Conclusion: We should perform effective adjuvant therapy to the patients without lymph node metastasis who are young or HER2 positive or High Histological Grade.

Prognosis-Prediction Model in Lymph Node-Negative Breast Cancer Patients Using Decision Tree Analysis

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Purpose: The aim of this study was to construct a prognosis-prediction model using multimarker in a decision tree.

Methods: Clinicopathological characteristics and disease free survival (DFS) rates were assessed in 328 lymph node-negative breast cancer patients.

Results: By univariate analysis, age, nuclear grade, estrogen receptor (ER), progesterone receptor (PgR), bcl-2, and Ki-67, were significant factors. Among these markers, both Ki-67 and bcl-2 were found to be independent prognostic factors in the Cox regression model. When these factors were subjected to decision tree analysis, Ki-67 was the best informative factor, followed by bcl-2, ER, and age. After reclassification using the decision tree, we defined the following criteria for high-risk group: 1) Ki-67 ≥ 10 and bcl-2-negative, 2) Ki-67 ≥ 10 , bcl-2-positive, and age < 35 years, and 3) Ki-67 < 10 and ER-negative. High-risk group had worse prognosis compared with low-risk group. The 5-year DFS rates for low- and high-risk group were 96.1% and 75.4%, respectively ($p < 0.01$). This prognosis-prediction model showed better results than did either the St Gallen classification or the use of Nottingham Prognostic Index. Our prediction model could divide the intermediate risk group by the St Gallen classification into two groups with significantly different DFS rates ($p < 0.01$).

Conclusion: In conclusion, this prognosis-prediction model using decision tree analysis was useful for defining high-risk lymph node-negative breast cancer patients.

Activation of mTOR Signaling Pathway in Breast Cancer and Its Correlation with Other Clinicopathologic Variables

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Purpose: Rapamycin, an mTOR inhibitor, and its analogues are currently being tested in clinical trials as novel-targeted anticancer agents. Pre-clinical studies using breast cancer cell lines have suggested that p-Akt or p-S6K1 expressing tumors as well as PTEN negative tumors were sensitive to rapamycin. The aims of this study were to determine the proportion of breast cancer that could be candidates of rapamycin treatment and to elucidate clinicopathologic characteristics and prognosis of potentially rapamycin-sensitive tumors.

Methods: We evaluated the expression of PTEN, p-Akt, p-S6K1 by immunohistochemistry in 122 breast cancer tissues. We analyzed the association of the expression of these proteins with other clinicopathologic variables and disease-free survival.

Results: PTEN negative tumors, p-Akt expressing tumors, and p-S6K1 expressing tumors constituted 4.1% (5/122), 41.0% (50/122), and 36.1% (44/122), respectively. The proportion of tumors that met the criteria of rapamycin sensitivity was 54.9% (67/122). We could not find any significant correlation between the expression of these proteins and other prognostic factors. However, the prognosis of tumors with p-S6K1 expression was significantly worse than that of p-S6K1 negative tumors.

Conclusion: Based on the status of PTEN, p-Akt, p-S6K1 expression as the predictor of rapamycin sensitivity, this study suggested that over 50% of breast cancer patients could be potential candidates of rapamycin treatment. In addition, p-S6K1 expression may constitute an independent prognostic factor of disease-free survival.

The Significance of Annexin A1 Expression in Breast Cancer

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Purpose: The expression of ANXA1 was found to be consistently reduced in human breast cancer. In this study we further characterized the expressional patterns of ANXA1 in breast cancer.

Methods: Human breast tissues were retrieved from the specimens of patients who had breast surgery or biopsy at Ewha University Medical Center. The expressional patterns of ANXA1 according to histopathologies was analyzed by immunohistochemical staining.

Results: Total of 106 women was included. A significant loss of ANXA1 staining was observed both in DCIS (n=7) and IDC (n=72) compared with normal epithelium (p=0.000). There was not significant difference for ANXA1 staining according to TNM stages (p=0.750), age (p=0.715), C-erbB2 (p=0.100), nodal status (p=0.800), and distant metastasis (p=0.489), there was but according to hormone receptor status (p=0.000), p53 (p=0.054), nuclear grade (p=0.000), and histologic grade (p=0.007) in invasive cancer. In addition, ANXA1 was strongly expressed in medullary carcinoma compared with lobular carcinoma (p=0.039), and mucinous carcinoma (p=0.057). In DCIS, the expression of ANXA1 was increased in high Van Nuys score (p=0.007). There was significant increase of ANXA1 expression after chemotherapy in the patients (n=13) who treated with neoadjuvant chemotherapy (p=0.013).

Conclusion: Our results showed that there was a significant decrease in expression of ANXA1 in breast cancer compared with either normal tissue or benign diseases. In addition, the results that ANXA1 expression was in correlation with some prognostic factors such as hormone receptor and nuclear/histologic grade can imply the value of ANXA1 as a new prognostic factor. As the significant difference between before and after chemotherapy of ANXA1 expression, we also expect that ANXA1 will be used as the index of therapeutic effect.

The Prognostic Significance of the Ratio of Positive Nodes to Removed Axillary Nodes in Breast Cancer Recurrence and Survival

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Purpose: The current study evaluated the prognostic impact of the ratio of positive nodes on recurrence and survival in node positive breast cancer.

Methods: A retrospective study was conducted on 743 axillary node positive breast cancer patients who had undergone modified radical mastectomy or conservation surgery and received systemic therapy between 1994 and 2003. Ten-year Kaplan-Myer (KM) disease free survival (DFS), overall survival (OS) rates stratified by the number of dissected lymph nodes, and percentage of positive lymph nodes were examined using different cut-off levels.

Results: The Median follow-up was DFS, OS rates correlated significantly with T-stage, lymphovascular invasion (LVI), estrogen receptor (ER), the number of dissected lymph nodes and the percentage of positive lymph node. The cut-off level at which the most significant difference in DFS and OS was observed was 20% positive lymph nodes (the 10-year KM DFS were 71.1% and 42.4% in women with <20% and ≥20% positive lymph nodes, respectively; $p < 0.001$). Lower OS rates were observed among patients who had ≥20% positive lymph nodes compared with patients who had <20% positive lymph nodes (OS: 54.0% vs. 76.8%, respectively; $p < 0.001$). In the multivariate analysis, the percentage of positive lymph nodes and T-stage were significant, independent factors associated with DFS and OS.

Conclusion: The presence of ≥20% positive lymph nodes was an adverse prognostic factor and may be used to identify patients at high risks of locoregional and distant recurrence who may benefit with adjuvant radiotherapy and more aggressive systemic therapy regimen.

Clinical Characteristics of Breast Cancer with Brain Metastases: 25-Years Experiences of Single Center

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Purpose: Central nerve system (CNS) metastasis is one of the feared complication of breast cancer and associated with poor prognosis. Purpose of this study is to clarify the clinical outcomes and prognostic factors of CNS metastasis from breast cancer.

Methods: Among 5,130 patients who were treated at SNUH from 1981 to 2006, CNS metastases were detected in 184 patients. We retrospectively reviewed the medical records, and analyzed their characteristics, treatment and the outcomes.

Results: Among 184 patients (median age:44 years), 157 patients (85.3%) have parenchymal metastasis only, 11 (6.0%) patients have LMS only and 16 patients (8.7%) have both. 155 (84.2%) patients had extracranial metastasis at the time of CNS metastasis. After detection of the CNS metastases, 160 patients (87.0%) received WBRT and 101 patients (54.9%) received chemotherapy. And the patterns of chemotherapeutic regimens have been changed as time goes by. The median survival after detection of CNS metastasis was 7.8 months. In univariate, brain parenchymal metastases had better survival than the other groups: 8.3 months, 3.3 months in LMS group and 6.9 months in combined metastases group ($p=0.012$). In addition, absence of extracranial metastasis (13.9 mo. vs 6.9 mo. in the extracranial metastasis, $p=0.029$), the performance status (PS) ($p<0.001$), adequate WBRT ($p=0.005$) and chemotherapy after CNS metastasis ($p<0.001$) affected the median survival. In multivariate, chemotherapy after CNS metastasis ($p<0.001$), PS ($p=0.019$), extracranial metastases ($p=0.023$) were independent prognostic factors.

Conclusion: Our results suggest that appropriate palliative chemotherapy is helpful for good performance status breast cancer patients even after detection of CNS metastasis.

Clinicopathologic Characteristics of Triple Negative Breast Cancer in Early Stages

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Purpose: Triple negative breast cancer (estrogen receptor-negative, progesterone receptor-negative, and c-erb B2 receptor-negative) is associated with high risk of recurrence and poor clinical outcome. Clinicopathologic characteristics of triple negative breast cancer is important to prediction of prognosis and decision of treatment guideline. We investigated the characteristics of triple negative breast cancer in early stages.

Methods: We reviewed the records of 821 early stage (stage I and II) breast cancer patients who was treated at our hospital from 1995 to 2005. We examined difference between triple negative group compared with non triple negative group in relation to clinicopathologic characteristics.

Results: Of 821 early stage breast cancer patients, 200 cases (24.4%) were of triple negative group. The mean age of triple negative group was 47.9 and non triple negative group was 48.9. Both histologic grade and nuclear grade of triple negative group were significantly higher than those of non triple negative group ($p=0.000$). Large tumors (T2 and T3) in triple negative group were significantly more than those in non triple negative group ($p=0.042$), but there was no significant difference in lymph node involvement between two groups ($p=0.933$). As of May 2007, with a median follow-up time of 50 months, there have been 50 local recurrences, 98 distant metastases, and 65 deaths. there were significant high rates of local recurrence ($n=21$, 10.5%) and death ($n=25$, 12.8%) in triple negative group ($p=0.006$, $p=0.010$ respectively).

Conclusion: Patients classified as triple negative breast cancer have poor pathologic findings and prognoses. Careful treatment and follow-up is important to triple negative breast cancer in early stages and further investigation is necessary to triple negative breast cancer.

Prognostic Evaluation of CD24 Expression in Invasive Ductal Carcinoma of Breast

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Purpose: CD24 is a small glycosylated cell surface protein that is considered to play a critical role in the metastasis of tumor cells through P-selectin. We aimed to determine prognostic value of CD24 expression in invasive ductal carcinoma of breast, and to investigate the relationship between histopathological parameters, estrogen and progesterone receptors, and c-erbB2 expressions.

Methods: CD24 expression was studied in 148 patients with invasive ductal carcinoma. All cases were reevaluated histopathologically and tissue microarray blocks were created. Immunohistochemistry was performed with monoclonal CD24 antibody.

Results: CD24 immunostain demonstrated cytoplasmic and membranous staining in 76 cases (51%). There was a significant correlation with c-erbB2 expression. No significant association was present between CD24 expression and patient age, tumor grade, stage, size, lymph node metastasis, estrogen and progesterone receptor status. Upon survival analysis, there was no statistical differences.

Conclusion: Our results suggest CD24 expression in invasive ductal carcinoma of breast may not be associated with clinical outcome and survival.

Clinical Characteristics of Triple Negative Breast Cancers

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Purpose: Breast cancer represent a heterogenous group of tumors that are diverse in behavior, outcome, and response to therapy. To reduce mortality from breast cancer, there is a desire to examine and characterize tumors of poor prognosis, to predict their biology, to ensure adequate therapy. We investigate the clinical characteristics of triple negative breast cancer (ER, PR, c-erb B2 negative, immunohistochemically: TN tumors) that lacks the benefit of targeted therapy.

Methods: From January 1995 to December 2002, 1,325 invasive breast cancer patients were operated. We investigated them retrospectively, who had the median follow-up for 62 months. We examined the differences between triple negative breast cancers compared with Non-triple negative breast cancers in relation to the clinicopathologic parameters, overall survival (OS), disease free survival (DFS). Statistical analysis was performed using SPSS (Chi-square, logistic regression, Kaplan-Meier).

Results: 213 (16.1%) cases among 1,325 patients were triple negative breast cancers. There were positive associations with younger age (below 35 years), poorly differentiated nuclear grade, negative axillary lymph nodes in TN tumors. Tumor size, histologic classifications, lymphovascular invasion were not significantly different between TN tumors and the other group. 199 patients (93.4%) were treated with chemotherapy. 26 cases (12.2%) of TN tumor experienced locoregional or systemic metastases, and 20 cases (9.4%) died. There was no significant difference of 5 year OS and DFS between TN tumors and the other group.

Conclusion: Triple negative breast cancers are associated with poorly differentiated nuclear grade and affect younger than Non-triple negative tumors. For the targeted therapy against triple negative tumor, we need to study the specific marker of these.

Prognostic Implication of CD44s Expression in Invasive Carcinoma of Breast

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Purpose: CD44s, the standard isoform of CD44, has been shown to be downregulated during malignant transformation of breast cancers. The purpose of this study is to determine the value of CD44s as prognostic marker for invasive ductal carcinoma of breast.

Methods: We analyzed the expression and prognostic significance of standard isoform CD44s using a breast cancer tissue microarray of 148 patients. CD44s, estrogen receptor, progesterone receptor and c-erbB2 were analyzed immunohistochemically and correlated clinical follow up.

Results: CD44s was expressed in 90 cases (61%). CD44s expression did not result in any difference in patient age, tumor stage, tumor grade, tumor size, lymph node metastasis, estrogen and progesterone receptor status and c-erbB2 expressions. Upon survival analysis, CD44s did not show any statistical correlation.

Conclusion: In summary, we could not find a clear relation between CD44s expression and prognosis of invasive breast carcinoma.

Comparative Analysis of TNM Stage and Volumetric T Stage as Predicting Factor of Breast Cancer Patients

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Purpose: The aim of this study is to assess the value of volumetric T stage as a new prognostic factor by reanalyzing the relationship between the tumor volume and disease free survival (DFS).

Methods: The study population consisted of 147 breast cancer patients between May 1997 and December 2003 who had taken diagnostic preoperative breast MRI. Patients with preoperative chemotherapy, diagnosed with DCIS or DCIS with microinvasion or who had extensive intraductal component over 50% were excluded. The tumor volume was measured by using the Web program using the breast MRI image. Tumor volumes were divided into Volumetric T1, T2, T3 according to a sphere with the diameter of 2 cm and 5 cm.

Results: The mean tumor size of the 147 patients was 2.8 cm and the mean tumor volume was 9,288 mm³. Mean follow up time was 67 months during which 17 patients had recurrence and 6 patients died. After analysis, volumetric T stage ($p=0.032$) proved to have a statistically significant influence on LN metastasis compared with T stage ($p=0.056$). According to the result of univariate analysis, age group (<35 ys or ≥ 35 : $p=0.0018$), T stage ($p=0.0316$), Volumetric T stage ($p=0.00003$), and N stage ($p=0.0018$) proved to be statistically significant prognostic factors for DFS. The result of multivariate analysis revealed that only age ($p=0.042$) and Volumetric T stage ($p=0.005$) had a statistical significance and the hazard ratio was 0.321 and 5.725 respectively.

Conclusion: Tumor volume proved to be an important prognostic factor in breast cancer patients. In addition to the TNM classification, volumetric T stage should also be considered in the assessment of breast cancer prognosis.

Expression Fractions of Estrogen Receptor and Progesterone Receptor Correlates to Prognosis in Stage I-III Breast Cancer

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Purpose: Expression fractions of estrogen receptor and progesterone receptor correlates to prognosis in stage I-III breast cancer.

Methods: We reviewed the clinical variables of 454 patients with stage I-III breast cancer patients treated at National Taiwan University Hospital (NTUH) in 1992-2000 and scored the ER and PR expressions by percentage of positive cells stained by immunohistochemistry on formalin-fixed paraffin embedded tissue sections. An ordinal scoring was assigned for each case by the percentage of positive-staining tumor cells (0, none; 1, 1-10%, 2, 11-30%; 3, 31-50%, 4, 51-70%; 5, 71-100%).

Results: A total of 454 patients with a median age of 49 years were included. To identify a clinically meaningful cut point for defining ER-positive tumors, we examined DFS curves for IHC scores of ER and PR for all patients. Our finding showed a gradually increasing DFS in tumors with higher IHC score of ER and PR. Best cut points of ER positivity (IHC score >1) and PR positivity (IHC score >1) were highly correlated with favorable DFS ($p=0.006$ and $p<0.001$, respectively) and OS ($p<0.001$ and $p<0.001$, respectively). In multivariate analyses, ER status remained significant to predict DFS ($p<0.001$) and OS ($p=0.017$). By this definition, the ER and PR positive rates were 67% and 68%, respectively.

Conclusion: The implementation of a fractioned immunohistochemical evaluation of hormone receptors may enhance the prognostic correlation in breast cancer patients.

Phase 2 Trial of Biweekly Gemcitabine in Combination with Weeklypaclitaxel (GT) for Treatment of Metastatic Breast Cancer

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Purpose: To assess the toxicity of a novel combination of gemcitabine and paclitaxel, as therapy for metastatic breast cancer. Single agent biweekly gemcitabine and weekly paclitaxel regimens appeared to offer more tolerability and possibly improved efficacy. Our hypothesis was to test a doublet based on the aforementioned schedules in an attempt to deliver more tolerable therapy preserving the efficacy of traditional (GT).

Methods: The study enrolled women with a diagnosis of chemotherapy naïve metastatic breast adenocarcinoma. All were treated with biweekly gemcitabine 1,500 mg/m² and weekly paclitaxel 80 mg/m². Cycle was 63 days. The toxicities were evaluated by CTC-3 criteria and response by RECIST criteria.

Results: Seven patients were enrolled in the trial, nine cycles of chemotherapy were delivered. Grade 3&4 hematologic toxicity was seen in all 9 cycles delivered. These toxicities required dose adjustments and omission of some doses. Stable disease was the best response. Four patients discontinued therapy due to toxicity, 2 patients due to progression, one died on therapy. The study planned to accrue a total of 51 patients in a two stage design stopping in stage 1 if 8/20 or more experienced grade 3/4 toxicity. After patient 7 experienced grade 3 toxicity, an analysis of the data showed there was only a 6.4% chance of avoiding one more grade 3/4 toxicity and a probability of failure 93.6%. Further accrual was stopped.

Conclusion: The studied schedule of GT appears to have unacceptable toxicity rates and is not recommended as an alternative dosing schedule to the standard schedule of the combination.

Preventive Effect of Pyridoxine against the Hand-Foot Syndrome Induced by Capecitabine

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Purpose: Capecitabine is one of the effective chemotherapeutic agents for breast cancer. It has response rate about 20% in anthracycline and taxane refractory cases, so it is widely used for advanced breast cancer patients. Hand-foot syndrome (HFSD) occur about half of the patients who received capecitabine that may cause cessation or dose reduction of the drug. Although oral pyridoxine (VB6) and/or urea ointment were usually applied, effective treatments or prevention methods of the hand-foot syndrome are not established. Herein, we evaluated oral pyridoxine as preventive method for capecitabine induced HFSD.

Methods: Forty patients who have received at least 3 courses of single agent capecitabine therapy (1,650 mg/m², administered for 21 consecutive days on a 28 day cycle; this is authorized regimen in Japan.) between July 2003 and February 2007 were reviewed retrospectively. Thirteen patients (32.5%) received prophylactic VB6 (60 mg/day per os daily) at the time capecitabine instituted (VB6 prophylaxis group).

Results: The median age of the patients was 60.5 years old (range 33-83) and the median administration period of capecitabine was 5 courses (range 3-21). HFSD occurred in 23 patients (57.5%). Although 20 patients out of 27 showed HFSD including 5 cases of grade 3 reactions in non-prophylactic group, only 3 patients out of 13 showed HFSD without grade 3 reactions in VB6 prophylaxis group.

Conclusion: This study suggested efficacy of prophylactic administration of oral VB6 for prevention of capecitabine induced HFSD. VB6 should be administered at the time of capecitabine therapy institutes.

A Case of Breast Cancer with Cartilaginous Metaplasia

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Purpose: This report describes a rare case of breast cancer with cartilaginous metaplasia.

Results: A 45-year-old woman was admitted because of a huge, rapid-growth tumor of the right breast. The tumor size was about 20 cm. Bilateral axillary lymph node swelling was not found. Mammography was poor study for a huge and firm tumor. Ultrasonography revealed a well-demarcated, hypoechoic mass including a large cystic area. A fine needle aspiration cytology revealed adenocarcinoma. Core needle biopsy was found cartilaginous metaplasia. ER, PgR and HER2/neu were negative. We diagnosed this tumor as a breast cancer with cartilaginous metaplasia. We chose the FEC100 for primary systemic therapy.

Conclusion: Breast cancer with cartilaginous metaplasia belongs to a special type of invasive carcinoma, and the incidence is very rare. We herein present our case and analysis of the literature.

A Case of Chylous Leakage after Axillary Lymph Node Dissection

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Introduction: Chylous leakage is a result of the thoracic duct damage and can occur after several surgical procedures such as neck and thoracic surgery. But it is an unusual complication occurring after axillary surgery. We experienced a case of chylous leakage after modified radical mastectomy and report the case here.

Case: A 38-year-old woman with invasive ductal carcinoma in the left breast underwent modified radical mastectomy. 4 cycles of neoadjuvant chemotherapy was done before the surgery. The surgical procedure was uneventful and a suction drain was left in the routine manner. Postoperatively, the serosanguineous drained fluid became 'milky' in the 4th postoperative day. The analysis of the fluid was compatible with chyle. (milky color, triglyceride 784 mg/dL, and total cholesterol 61 mg/dL) Initially, conservative management was tried, but the daily output was increased in the 7th postoperative day. So we reexplored the axilla and observed that the clear fluid was running from a single duct just below the lateral pectoral bundle branch. We performed mass ligation of the duct and the suspicious site 3-4 cm below the duct. The subsequent drain output was decreased and we removed the drain after 9 days.

Discussion: Rarely, injury to the thoracic duct or its branch can occur during the axillary surgery. Chylous leakage is diagnosed by the typical 'milky' drained fluid. Although the initial management of the chylous leakage was tried conservatively, surgical treatment should be considered if the amount of output were increased.

Neuroendocrine Breast Carcinoma Arising from a Pregnant Woman: A Case Report

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Introduction: Neuroendocrine breast carcinoma is an uncommon neoplasm. It can be confirmed by means of specific neuroendocrine markers, such as chromogranins and synaptophysin. We describe the case of a patient who is pregnant with neuroendocrine breast carcinoma.

Case: A 39-year-old woman of thirty-two weeks pregnant was transferred to our Institution on May 2007 from a local breast clinic with a left breast mass which was revealed as invasive ductal carcinoma on core needle biopsy. Physical examination disclosed a well demarcated, movable lump of 5.5 cm in size in the upper-outer quadrant of the left breast and there was no palpable axillary mass. On sonogram the tumor was located the 2 o'clock direction, 3 cm from the nipple, 5 cm in size. Then breast-conserving surgery with axillary node dissection was performed. Histopathologic diagnosis was neuroendocrine carcinoma, 5.0 cm in size with histologic grade 3 and nuclear grade 3 without lymphovascular tumor emboli. And axillary lymph nodes were positive in 2 of 29. Immunohistochemistry for cytokeratin was positive, as were the neuroendocrine markers: chromogranin and synaptophysin. The estrogen receptor and progesterone receptor were negative. Two weeks after operation, she gave birth by induced vaginal delivery. Two weeks after delivery, she received anthracycline based adjuvant chemotherapy.

A Case of Osteonecrosis of the Jaw Associated Bisphosphonates for the Management of Bone Metastases from Breast Cancer

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Purpose: Bisphosphonates (BPs) are often used for osteoporosis, cancer-associated hypercalcemia and osteolytic bone metastasis. We report an osteonecrosis of the jaw (ONJ) in breast cancer patient with bone metastases receiving long-term treatment with BPs.

Results: A 70-year-old woman underwent modified radical mastectomy for her left breast cancer and received oral 5-fluorouracil derivatives for 2 years in other hospital. Eleven years after the operation, she came to our hospital because of spinalgia and was diagnosed as having breast cancer recurrence with multiple metastases of stomach, liver, multiple lymph nodes and spines. After surgery for spine metastases, combination therapy with trastuzumab (initially 170 mg/body followed by two or more cycles of 85 mg/body) every week and docetaxel (100 mg/body) every 3 weeks and BPs (90 mg/body) every 4 weeks were given. About 1 year and 4 months later, she complained of the pain in her right maxilla. After conservative treatment, biopsy of her right maxilla revealed ONJ.

Conclusion: Medical oncologists need to recognize ONJ as a serious side effect of BPs and to make informed consent to the patients and a close consultation with dentists and oral and maxillofacial surgeons for administration of BPs.

Breast Cancer in Three Women Associated with Von Recklinghausen's Disease

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Type 1 neurofibromatosis (NF1), also known as Von Recklinghausen's disease, is a common autosomal dominant genetic neurocutaneous disorder. Persons with NF1 have an increased risk of malignancy compared with the general population. But there are few reports of neurofibromatosis combined with the breast cancer. We experienced three cases of breast cancer combined with Type 1 neurofibromatosis. We report these unusual cases.

Metastatic Tumor Progressed on Imatinib (Gleevec) in Two Patients with C-Kit-Positive Metastatic Malignant Phyllodes Tumor of Breast

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Purpose: Phyllodes tumor of breast is fibroepithelial neoplasm, comprises less than 1% of all breast tumors. About 10 to 15% of phyllodes tumor is malignant and could metastasize to lungs, bones or liver. c-kit (CD117) immunohistochemical reactivity was noted in epithelial and stromal components in up to 66% of cases and predicted recurrent disease, which suggested c-kit receptor mediated tyrosine kinase involvement in the pathogenesis of phyllodes tumors.

Results: Recently two patients were seen at NCC, who presented with rapidly progressive metastatic phyllodes tumors in the right lung in one 56-year-old patient and in the soft tissue wrapping around the upper C-spine in the other 43-year-old patient. Imatinib (Gleevec) at 800 mg per day, p.o. was tried with the lack of therapeutic options and in the light of moderate to strong c-kit positivity. However, the disease progressed further at the same pace on the drug that it was stopped after 3 weeks for one patient and 10 days for the other patient. One died of airway obstruction by tumor mass, and the other is alive with severe respiratory distress due to huge lung metastases and accompanied hemolytic anemia developed since 6 months.

Conclusion: Although our experience with imatinib on two patients is disappointing, further trial with more patients is required to give a full analysis of imatinib in this disease.

Malignant Breast Tumours in Asians Adolescent Girls

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Purpose: To determine the incidence of breast malignancy in Asian adolescent girls, and to discuss any peculiar clinical features, treatments, and outcomes.

Methods: From a prospectively collected database between 1990-2006 of 1270 women treated for breast malignancy at Changi General Hospital.

Results: There were four patients who were aged 20 years and below. Their mean age was 18.3 years (17-20). All did not have any family history of breast cancer or other risk factors. All presented with clinically benign breast lumps. Ultrasound assessment for two showed benign features, one was indeterminate. Histological diagnosis was obtained after excision biopsy and showed malignant pathology of different types (ductal carcinoma, DCIS, Malignant phylloides and sarcoma). All underwent simple mastectomy and axillary dissection. Immediate reconstruction was performed for three. Adjuvant therapy was based on histology. Median follow-up is 40.5 months (8-136), and there have been no recurrences.

Conclusion: From this study, the incidence of breast malignancy in Asian adolescent girls is 0.003%. Breast lumps in adolescent girls are often presumed to be benign in view of the rarity of malignancy. Good results are possible with the appropriate treatment.

A Trial of Total Supportive Care for Breast Cancer Patients with Massive Skin Invasion

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Purpose: Although early detection of breast cancer increases, sometimes there are patients who make the first visit after massive skin invasion has appeared. Ordinary, primary systemic chemotherapy is indicated for those patients. However, the patient's quality of life (QoL) was prominently worsened because of bleeding, secretion and odor smear from the exposed tumor until anti-cancer therapy achieves good response. On the other hand, almost all of the chemotherapies for breast cancer become to perform at the outpatients department. Therefore, treatment and care of skin lesion is entrusted to the patient and her family then they suffered from many matters for example how to take a bath. A treatment in an outpatient department may rather decrease QoL for such a case.

Methods: We have been trying to establish home and community based continuous care for the patients who need daily care of the skin lesion in the relation of doctors, nurses including oncology nurse, WOC nurse and health visitor, medical social workers and local clinic.

Results: We have intervened to 4 patients. All of them satisfied our comprehensive care and felt decreasing odor smear after instruction for local lesion care by WOC nurse.

Conclusion: A medical team approach must be performing not only anti-cancer therapy but also all matters which correlated with the disease.

The Effects of Foot Reflex Therapy and Spiritual Nursing Intervention on Anxiety and Stress on Mastectomy Patients

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Purpose: The research design was a non-equal control group non-synchronized design. The study method had been done by investigation the experimental group and control group through the questionnaire on 38 patients who had been out patients at Saegyaero hospital in Busan Korea from July 23 to September 28, 2006.

Methods: The foot reflex therapy and spiritual nursing intervention was provided to the experimental group for 30 minute, 8 times twice a day at in hospital room. Dependent variables were measured by Spielbergs Trait-state anxiety inventory, visual analog scale and serum cortisol. The collected data were analyzed χ^2 test t-test with SPSS.

Results: The results were summarized as follows.

1. Hypothesis 1: The first hypothesis that “There will be significant difference of anxiety score in the experimental group and control group” was supported ($t = -3.39$, $p = 0.003$).
2. Hypothesis 2: The second hypothesis that “There will be significant difference of stress in the experimental group and control group” was supported ($t = -3.91$, $p = 0.001$).
3. Hypothesis 3: The third hypothesis that “There will be significant difference of serum cortisol in the experimental group and control group” was supported ($t = 3.52$, $p = 0.002$).

Conclusion: In conclusion, the foot reflex therapy and spiritual nursing intervention was found to reduces anxiety, stress in mastectomy patients. So, the foot reflex therapy and spiritual nursing intervention had been judged the nursing intervention to improve their emotional problem in mastectomy patients.

Impacts of Implementing a Decrease of Payment Rate for Breast Cancer Patient

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Purpose: To investigate the impacts of the introduction to breast cancer patient's own medical payment rate decreasing system upon medical utilization and health expenditure.

Methods: Examined the Electronic Data Interchange (EDI) of medical treatment benefit expenses, arising from breast cancer (C50~C509), metastatic diagnosis disease (C76~C80), for 6 months from January to June 2005, before the after mentioned system was implemented, and for 6 months from January to June 2006, when the system was implemented.

Results: Concerning the change of average medical service use and treatment expenses per patient during 6 months, the number of hospitalization days decreased 5.2% from 18.54 days to 17.58 days, the hospitalization treatment expenses rose 4.3% from 3,454,770 won to 3,603,980 won, after the above mentioned system was implemented. The difference in treatment expenses per patient during 6 months before and after the system did not exhibit a significant result. The change in the number of hospitalization days decreased after the implementation of system and it was statistically significant result. A multiple regression analysis was used to find significant impacts on decrease of the number of hospitalization day during six months. The implementation of the system was more statistically significant in group without metastatic disease rather than with, Seoul than Do, corporation than personal.

Conclusion: Government policy carried out as a part of strengthening guarantee will affect positively in the impacts of implementing an decrease of the Patient's Payment Rate on the medical utilization and health expenditure for Breast Cancer patient.



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Kang, Daehee	GBCC01-020	119	Kim, Eun Mi	GBCC01-081	180
Kang, Daehee	GBCC01-021	120	Kim, Eun Mi	GBCC01-091	190
Kang, Daehee	GBCC01-022	121	Kim, Eun Shim	GBCC01-025	125
Kang, Han Sung	GBCC01-099	198	Kim, GiYon	GBCC01-003	101
Kang, HeeJoon	GBCC01-070	169	Kim, GiYon	GBCC01-005	103
Kang, Hye Jin	GBCC02-004	203	Kim, GiYon	GBCC01-031	129
Kang, Hyun Jong	GBCC02-017	216	Kim, H	GBCC01-042	140
Kang, Jason Jongho	GBCC01-037	135	Kim, Haeyoung	GBCC01-064	162
Kang, Su Hwan	GBCC01-081	180	Kim, Hae-Young	GBCC02-065	269
Kang, Su Hwan	GBCC01-091	190	Kim, Hae-Young	GBCC02-070	275
Kang, Sung Soo	GBCC01-023	122	Kim, HakHee	GBCC02-016	215
Kang, Sungsoo	GBCC01-090	189	Kim, Hee Jeong	GBCC01-012	111
Kang, Sung Soo	GBCC02-073	279	Kim, Hee Jeong	GBCC01-066	165
Kang, Sung Soo	GBCC02-085	292	Kim, Hee Jeong	GBCC01-089	188
Kang, Sun Hee	GBCC02-007	206	Kim, Hee Jeong	GBCC02-002	201
Kang, Sun Hee	GBCC02-083	290	Kim, Hee Jeong	GBCC02-016	215
Kato, Yasuyuki	GBCC02-029	228	Kim, Hee Jeong	GBCC02-022	221
Kato, Yasuyuki	GBCC02-090	297	Kim, Hee-Jun	GBCC02-082	289
Kato, Yasuyuki	GBCC02-098	305	Kim, Hee Jung	GBCC01-060	158
Kawajiri, Hidemi	GBCC02-029	228	Kim, Hee-Seung	GBCC02-049	251
Kawajiri, Hidemi	GBCC02-090	297	Kim, Heesook	GBCC01-090	189
Kay, Chul Seung	GBCC01-094	193	Kim, Ho	GBCC01-020	119
Kazuhiro, Takeuchi	GBCC01-072	171	Kim, Hun-Soo	GBCC02-015	214
Keam, Bhumsuk	GBCC02-082	289	Kim, Hye Gyong	GBCC02-005	204
Kenjiro, Kimura	GBCC01-072	171	Kim, Hye Gyong	GBCC02-009	208
Kent, Mencer	GBCC02-013	212	Kim, Hyeon Sook	GBCC02-014	213
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Kil, Won-Ho	GBCC01-058	156	Kim, Hyesun	GBCC01-090	189
Kil, Won-Ho	GBCC01-063	161	Kim, Hye-Won	GBCC02-015	214
Kil, Won-Ho	GBCC02-025	224	Kim, Hyo Lim	GBCC02-017	216
Kil, Won-Ho	GBCC02-081	288	Kim, Hyun-Ah	GBCC01-043	141
Kim, Ae-Ree	GBCC02-003	202	Kim, Hyun-Ah	GBCC01-073	172
Kim, Bo-Ram	GBCC02-038	239	Kim, Hyun-Ah	GBCC01-100	199
Kim, ChangHee	GBCC01-003	101	Kim, Hyun-Ah	GBCC02-079	286
Kim, ChangHee	GBCC01-005	103	Kim, Il Han	GBCC01-041	139
Kim, ChangHee	GBCC01-031	129	Kim, In Ah	GBCC01-041	139
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Kim, Dae Shick	GBCC01-063	161	Kim, In-Sook	GBCC02-051	253
Kim, Dal Sook	GBCC02-042	243	Kim, J	GBCC01-042	140

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Kim, Jae Sung	GBCC01-093	192	Kim, Sang Hyo	GBCC02-095	302
Kim, Jee Hyun	GBCC01-093	192	Kim, Sangmin	GBCC01-051	149
Kim, Jee Hyun	GBCC02-082	289	Kim, Sangwon	GBCC02-074	280
Kim, Jeongeun	GBCC02-064	268	Kim, Seok Won	GBCC01-099	198
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Kim, Jong Bin	GBCC01-052	150	Kim, Sung-Won	GBCC01-013	112
Kim, Jong Bin	GBCC01-053	151	Kim, Sung-Won	GBCC01-014	113
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Kim, Jong Im	GBCC02-068	273	Kim, Sung Won	GBCC02-018	217
Kim, Jong-Seok	GBCC01-049	147	Kim, Sung Won	GBCC02-038	239
Kim, Jong-Seok	GBCC01-050	148	Kim, Sung Won	GBCC02-041	242
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Kim, Jung Han	GBCC02-081	288	Kim, Sung Yong	GBCC01-074	173
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Kim, Mi-Yea	GBCC02-044	245	Ko, Eunyong	GBCC01-051	149
Kim, Nam-Cho	GBCC02-049	251	Ko, Eunyong	GBCC01-052	150
Kim, Sairhee	GBCC01-010	109	Ko, Eunyong	GBCC01-053	151
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Kosugi, Chihiro	GBCC02-008	207	Lee, Insook	GBCC02-034	235
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Ku, Hye-young	GBCC02-099	306	Lee, Jae-hoon	GBCC01-085	184
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Kweon, Gi-Ryang	GBCC01-049	147	Lee, Jin Sun	GBCC02-009	208
Kweon, Gi-Ryang	GBCC01-050	148	Lee, Jinyong	GBCC02-074	280
Kweon, Gui Yung	GBCC01-012	111	Lee, Ji Shin	GBCC01-045	143
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Kwon, Oc Ju	GBCC02-043	244	Lee, Ji-Young	GBCC01-022	121
Kwon, Youngmee	GBCC01-099	198	Lee, Jong Eun	GBCC01-019	118
Kwon, Young Mi	GBCC02-096	303	Lee, Jong Won	GBCC01-013	112
Kwun, Koing Bo	GBCC02-007	206	Lee, Jong Won	GBCC01-051	149
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Lee, AeKyung	GBCC02-075	281	Lee, Jong Won	GBCC01-053	151
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Lee, Chunghan	GBCC01-035	133	Lee, Jong Won	GBCC02-018	217
Lee, Chunghan	GBCC01-088	187	Lee, Jong Won	GBCC02-071	277

Lee, Jong Won	GBCC02-078	285	Lee, Su Min	GBCC01-048	146
Lee, Jung Ah	GBCC02-072	278	Lee, Sun Ah	GBCC02-080	287
Lee, Jung-Lim	GBCC02-035	236	Lee, Sung Sook	GBCC01-039	137
Lee, Jung-Lim	GBCC02-064	268	Lee, Sun Mi	GBCC02-069	274
Lee, JungSun	GBCC01-012	111	Lee, Wei-Chung	GBCC02-076	283
Lee, JungSun	GBCC01-066	165	Lee, Won Chul	GBCC01-048	146
Lee, JungSun	GBCC01-089	188	Lee, Wonhee	GBCC02-034	235
Lee, JungSun	GBCC02-002	201	Lee, WooHo	GBCC01-072	171
Lee, JungSun	GBCC02-016	215	Lee, Woomi	GBCC02-050	252
Lee, JungSun	GBCC02-022	221	Lee, Young Don	GBCC02-093	300
Lee, Keun Seok	GBCC01-099	198	Lien, Huang-Chun	GBCC02-076	283
Lee, Keun Seok	GBCC02-096	303	Lien, Huang-Chun	GBCC02-088	295
Lee, Kwang-Man	GBCC01-098	197	Lim, Cheol-Wan	GBCC01-056	154
Lee, Kwang-Man	GBCC02-015	214	Lim, Cheol-Wan	GBCC01-074	173
Lee, Kwang-Man	GBCC02-040	241	Lim, H.I.	GBCC01-059	157
Lee, Kyoung-Mu	GBCC01-019	118	Lim, Hye-In	GBCC01-058	156
Lee, Kyoung-Mu	GBCC01-020	119	Lim, Hye-In	GBCC01-063	161
Lee, Kyoung-Mu	GBCC01-021	120	Lim, Hye-In	GBCC02-081	288
Lee, KyungHi	GBCC02-045	246	Lim, Jae-Young	GBCC01-087	186
Lee, KyungHi	GBCC02-047	248	Lim, Jae-Young	GBCC02-038	239
Lee, Kyung-Min	GBCC01-051	149	Lim, Jae-Young	GBCC02-041	242
Lee, Kyung-Min	GBCC01-052	150	Lim, Joung Sun	GBCC02-066	271
Lee, Kyung-Min	GBCC01-053	151	Lim, Joung Sun	GBCC02-067	272
Lee, Kyung-Min	GBCC01-054	152	Lim, Jung Soon	GBCC02-046	247
Lee, Min A	GBCC02-093	300	Lim, KR	GBCC02-097	304
Lee, Min-Hyuk	GBCC01-011	110	Lim, Kyu	GBCC01-049	147
Lee, Min-Hyuk	GBCC01-056	154	Lim, Kyu	GBCC01-050	148
Lee, Min-Hyuk	GBCC01-074	173	Lim, Woosung	GBCC01-066	165
Lee, Min Kyuk	GBCC01-018	117	Lim, Woosung	GBCC01-089	188
Lee, Myongsoon	GBCC02-050	252	Lim, Woosung	GBCC02-002	201
Lee, Myung Kyung	GBCC02-059	263	Lim, Woosung	GBCC02-016	215
Lee, Nan Joo	GBCC02-095	302	Lim, Woosung	GBCC02-022	221
Lee, Ran	GBCC01-026	126	Lin, Ching-Hung	GBCC02-076	283
Lee, Ryung-Ah	GBCC01-043	141	Lin, Ching-Hung	GBCC02-088	295
Lee, Sang Dal	GBCC01-034	132	Low, SC	GBCC02-048	250
Lee, Sangdal	GBCC01-092	191	Low, SC	GBCC02-097	304
Lee, Sang Hun	GBCC01-070	169	Lu, Yen-Shen	GBCC02-076	283
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Lee, Seung Ah	GBCC02-023	222	Menzel, Christian	GBCC01-077	176
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Moon, Nan-Mo	GBCC01-073	172	Noh, Dong-Young	GBCC01-022	121
Moon, Nan-Mo	GBCC01-100	199	Noh, Dong-Young	GBCC01-027	135
Moon, Nan-Mo	GBCC02-079	286	Noh, Dong-Young	GBCC01-051	149
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Moon, Woo Kyung	GBCC02-019	218	Noh, Dong-Young	GBCC01-053	151
Moon, Woo Kyung	GBCC02-020	219	Noh, Dong-Young	GBCC01-054	152
Moon, Woo Kyung	GBCC02-021	220	Noh, Dong-Young	GBCC01-061	159
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Nam, Seok-Jin	GBCC01-058	156	Oh, Ki Keun	GBCC02-087	294
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Nam, Seok-Jin	GBCC01-064	162	Oh, Pok-Ja	GBCC02-039	240
Nam, Seok Jin	GBCC02-006	205	Oh, Se Jeong	GBCC01-094	193
Nam, Seok-Jin	GBCC02-025	224	Oh, Se Jeong	GBCC02-017	216
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Paik, Nam-Sun	GBCC02-028	227	Park, SoMi	GBCC01-031	129
Paik, Nam-Sun	GBCC02-079	286	Park, Soon-Tae	GBCC01-038	136
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Park, Hye Rim	GBCC01-016	115	Ro, Jungsil	GBCC02-096	303
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Park, Jun Ho	GBCC01-016	115	Santen, Richard	GBCC01-071	170
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Seo, Hyung-Il	GBCC01-079	178	Son, Eun Joo	GBCC02-087	294
Seo, Hyung-Il	GBCC01-080	179	Son, Eun Ju	GBCC02-012	211
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Shin, HeeJung	GBCC02-016	215	Sukumar, Sara	GBCC01-045	143
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