Conclusions: As ductal lavage offers a bigger amount of cells from the final duct-lobe unit, it can be very useful in high risk women. The technique can help ih the early diagnosis of breast cancer and to the management of them with tamoxifen. Our study will be continued with new patients and observation of these 85.

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Breast cancer in women over 80's: a case report of 14 patients

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Background: Breast cancer is a common cancer in women. The 10-year survival rate for stage II is 66% in the general population. The management of early disease in women over 80 year-old is a major challenge for oncologists and gynecologists. The important role of comorbidities and their effect on life expectancy also need to be taken into account when making treatment decisions. The knowledge about possible differences in the biology and clinical outcomes of breast cancer in women over 80 year-old is limited in Brazil. In this study, we have explored the clinical and biologic characteristics of elderly women with breast cancer in two private clinics in the south of Brazil, where the prevalence of breast cancer is 127/100.000.Material and MethodsThe medical records of fourteen patients with $\geqslant$80 year-old, from 2 private clinics, with confirmed breast cancer, were reviewed. The method of diagnosis, the initial stage of disease at the time of diagnosis, hormone receptor status, type of treatment and survival rate after treatments were evaluated. Statistical description and Fisher's exact test were performed for statistical analysis.ResultsThe average age at the diagnosis was 82 year-old. Ductal carcinoma was the most prevalent histological type (85.7%). The average size of tumor at diagnosis was 2.8 cm, and the stage II was the average clinical stage at diagnosis. The survival rate was 64.3% in 29 months. Eleven patients (78.6%) were submitted to surgery. None of them died within the first 12 months. Tumor size at diagnosis (cut-off 1.9 cm), status of estrogen and progesterone receptors, the use of a diagnostic image (mammography/ultrasound), presence of comorbidity (cut-off $\leqslant$1), stage of disease (cut-off $\leqslant$ stage I), and surgery were not correlated with a better outcome (all $p > 0.05$). ConclusionIn our sample of women over 80 year-old, the survival rate is similar to the general population irrespectively of disease status. Despite of the presence of comorbidities, none of the patients died within 1 year after surgery.

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Enhancing access to care and treatment by engaging and strengthening health systems in low-resource settings: a public–private partnership to improve breast cancer care in Ethiopia

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Background: The Ethiopia Breast Cancer Pilot Project (BCPP) was established to create and demonstrate a model for strengthening health care systems to treat breast cancer in developing countries. It was funded by AstraZeneca through a grant to Axios Foundation.

Methods: BCPP developed a model to strengthen health systems by empowering local leaders and providing direct support to enhance major components of breast cancer care (e.g., radiotherapy, pathology, pharmacy, community outreach) in Addis Ababa's largest teaching hospital (Tikur Anbessa Hospital). Where appropriate, international standards of practice were used to develop locally relevant guidelines and processes designed to enhance access to care and treatment for breast cancer patients.

Results: BCPP began in 2005 with an initial focus on expanding health systems that support breast cancer diagnosis and treatment. Achievements to date include creation of clinical guidelines, obtaining radiology (mammography & ultrasound) equipment, building laboratory capacity for ER/PR testing, training clinicians and support staff, establishing access to tamoxifen and anastrozole and implementing monitoring and evaluation systems. In addition, a cancer patient advocacy and outreach affiliate was established by the set up of the Ethiopian Cancer Association (ECA), and by creating links with related referral institutions and government agencies. As anticipated for a low-resource country with poor health infrastructure, the program has faced challenges around training, introduction of new concepts and technologies, establishing and maintaining effective supply chain, and notably drawing patients into care at an earlier stage of cancer when treatment may be most beneficial. Engaging stakeholders and key opinion leaders in solving and managing these challenges has increased sustainability and investment in the project. Over 500 patients have benefited directly from BCPP services to date and patient navigation through complex clinical and technological systems in a culture that often stigmatizes cancer has dramatically improved.

Conclusions: BCPP has successfully demonstrated that health systems supporting cancer treatment and care in a very low-resource environment can be significantly and rapidly strengthened through effective stakeholder engagement, leveraging public and private political will and resources, and collaborative technical assistance that prioritizes local decision-making and management.

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Guidelines for bone health in postmenopausal women (PMW) with hormone-sensitive breast cancer (HSBC) receiving adjuvant aromatase inhibitor (AI) therapy

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Background: AIs are approved for PMW with HSBC. Studies have shown that all AIs (anastrozole, exemestane, or letrozole) decrease bone mineral density (BMD) and increase bone turnover markers, increasing risk for osteoporosis and fractures compared with placebo or tamoxifen, regardless of treatment setting.

Methods: A systematic literature review was performed to identify factors that contribute to the increased fracture risk observed in HSBC patients as well as recommendations for treatment of AI-associated bone loss (AIBL).

Results: As BMD testing is not readily available to all patients, additional evidence-based guidance to assess fracture risk and direct treatment is important. Risk factors in patients with breast cancer are AI therapy, T-score < -1.5, age >65, family history of hip fracture, history of personal fracture after age 50, oral corticosteroid use >6 months, low body mass index (<20 kg/m^2), and smoking. HSBC patients at risk of developing AIBL should be considered for preventative bisphosphonates (BP) treatment. AIBL stabilizes with completion of therapy and is attenuated when zoledronic acid (ZOL) is added to the treatment regimen. Randomized clinical trials support ZOL 4 mg every 6 months for prevention of AIBL when a patient is identified to be at risk, and data with other bisphosphonates are emerging.

Conclusions: All PMW initiating AI therapy should receive calcium (1200 mg/d) and vitamin D (400–600 mg/d) supplements. Concomitant ZOL can attenuate AI-associated bone health risks. Current guidelines rely solely on the presence of osteoporosis (BMD < -2.5) to guide bisphosphonate intervention. Yet, as 80% of fractures occur in osteopenic women, this threshold appears inadequate for averting fractures in PMW with HSBC. Patients receiving ZOL should have BMD monitored yearly. BP should be used for at least 2 years and possibly for as long as AI therapy is continued. It would be prudent to give ZOL 4 mg twice yearly to PMW who are taking AIs and have a T-score < -2.0 or have any 2 of the following risk factors: T-score < -1.5, age >65 years, family history of hip fracture, personal history of fracture after age 50, smoking, or oral corticosteroid use >6 months.

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Male breast cancer in Chinese population – a 10 year review

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Background: Breast cancer is uncommon in men, occurring in 1% of the male population based on Western data. There is limited knowledge about the natural history and prognosis of male breast cancer in Chinese population. This study aims to perform a 10 year review of the clinical presentation and outcome of male breast patients in Hong Kong.

Materials: A retrospective study of patients with male breast cancer treated in Hong Kong from January 1995 to December 2005 was performed.

Results: A total of 77 male breast cancers were treated in eight hospitals during this 10 year study period. The mean age at diagnosis was 65 years old. Majority (92.6%) presented with a palpable breast lump. Only 3 men had gyanecomastia. Only 3.3% had a family history of breast cancer. All patients (7 unknown) underwent mastectomy except for 1 who has wide local excision (sarcoma). 51.4% of these patients also had axillary dissection performed. 85.7% of these were invasive carcinoma of which 1 was invasive lobular carcinoma, 2 were mucinous carcinoma, 5 were invasive papillary carcinoma and the rest were invasive ductal carcinoma. 12.9% were in-situ carcinomas, where 7 were intraductal papillary carcinoma and the rest were ductal carcinoma in-situ. Of the

invasive tumors, 77.2% were classified as Grade II and above. 23.4% of these patients had nodal involvement and the most common stages of presentation were Stage 1 (32.9%) and Stage 2 (35.7%). Majority of the tumors were oestrogen (95.5%) and progesterone (81%) receptor positive and 27.9% and 18.6% were cerbB2 score 3+ and 2+ respectively. Where treatment data was available, 90.2% patients with ER positive tumors received tamoxifen. 18.2% received adjuvant chemotherapy and 40.3% received radiation therapy. The mean follow up time was 55.4 (2–178) months. The 2-year vs. 5-year disease free and overall survival were 93.2% and 85.9% vs. 73.8% and 74.2% respectively. Interestingly 15 patients also had a second primary cancer not of breast origin. These patients had a significantly worse overall survival ($p = 0.07$).

Conclusions: Male breast cancer in Chinese men is rare and present at an old age but at an early stage (Stage 1 and 2). Although a majority of our cohort did not have family history of breast cancer, there was a high incidence of second primary cancer not of breast origin. Further investigation with genetic study in this group of patients is likely to be of relevance.

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Body weight and the risk of breast cancer in BRCA1/2 families – the GEO-HEBON study

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In the general population, an inverse association has been observed between both body weight and body mass index (BMI) and the risk of premenopausal breast cancer, whereas body weight and BMI increase the risk of postmenopausal breast cancer. So far, association between body weight and BMI and breast cancer risk in BRCA1/2 families is unknown.

We assessed the association between body weight and breast cancer in a large series of 485 BRCA1/2 families, consisting of 918 BRCA1/2 carriers and 142 obligate carriers from the GEO-HEBON study, a retrospective nationwide cohort study. Information on hormonal/lifestyle factors was obtained from a self-administered questionnaire. Information on breast and ovarian cancer and on preventive surgical measures was verified via the PALGA database (Pathological Anatomy National Automated Archive) and the Netherlands Cancer Registry until August 2007.

Participants were asked to report current body weight and height and body weight from age 18 years onwards in 10-year age groups (ages ranging from 20−29, 30−39, 40−49, 50−59 and 60−69 years), excluding pregnancy in these periods. Current body weight and height were used to compute current BMI in kilograms per squared meters. Analyses will be preformed to examine the effect of body weight and BMI at age 18 years and censoring, changes in body weight (20 years of age till censoring), and height on breast cancer risk in BRCA1/2 families. All analyses will be stratified according to menopausal status. Hazard ratios will be estimated using a Cox-regression approach stratified for gene and birth cohort. Results will be presented.

Wednesday, 16 April 2008 12:30–14:30

POSTER SESSION

Molecular biology, markers

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Proteomics in mammary cancer research

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Background: This study combines a summary of proteomics techniques and protein analysis (in mammary cancer) with a report of expressed and up-regulated proteins in benign and malignant mammary tissues.

Till now, only few reports of proteomic research for mammary cancer could be found, including the techniques of two-dimensional gel electrophoresis (2-DE), MALDI/ESI/TOF and ESI/MS, browsing the PubMed database. Human carcinoma cell lines, mouse material or human serum were the most exercised materials for these studies. Only a few of them used native tissues from patients with mammary carcinomas.

The aim of this study was to search for more, not well-established (up-regulated) proteins in mammary cancer in the mean and low molecular weight (MW) range, to figure out the role of post-translational modification in biologic processes and to recognize newer pathways.

Material and Methods: Tissue samples ($n = 26$), originated from 10 healthy female donors (benign mammary tissue; K01–K10; control group) and 16 donors who had developed mammary carcinomas of a ductal type (P01–P16), were snap-frozen in liquid nitrogen and stored at −70ºC till analysis. High resolution 2-DE was performed, according to the literature, using a pH gradient from 2−11. The most abundant spots representing the selected variant spot groups were manually picked in a clean bench to provide sufficient material for MALDI-MS, as well as nano-liquid chromatography-electro spray ionization-mass spectrometry (nano-LC-ESI-MS) based protein identification.

Results: Beside hypothetical proteins a number of transcription factors, such as zinc finger proteins (ZNFs), and not well-investigated (high significant) proteins, e.g., elongation factor 1-alpha 1 (eEF1A1), were identified by mass spectrometry (MS). eEF1A1, expressed in the membrane of mammary carcinomas, is involved in gene expression/translational elongation and has a GTPase activity and an oncogenic potency.

Another protein, for example, calgizzarin (S100A11; S10AB human), which is involved in carcinoma invasion and tumor metastases, could be determined as over-expressed in the cytosol of mammary cancer tissues. It is also concerned with the regulation of numerous cellular processes such as cell cycle progression and differentiation.

Conclusion: With this study, we want to demonstrate that proteome analyses provide a powerful tool for detecting potential and new biomarkers, which could be validated for diagnostic and clinical features of mammary carcinomas.

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Approaching molecular classification of breast cancer by using a panel of molecular tumor markers

P. Sinn[1], S. Aulmann[1], P. Schirmacher[1]. [1]*University of Heidelberg, Gynecopathology, Heidelberg, Germany*

Background: Gene expression profiling has resulted in the definition of distinct and robust clusters of distinct types of breast cancer (luminal A and B, erbB2-like, basal-like, normal breast-like). However, the question how to transform this classification into clinical practice is quite uncertain.

Materials and Methods: We have used a panel of 6 immunohistological markers on primary invasive breast cancers and collected data from 3733 tumors. The panel includes ER (1D5), PgR (PgR636), HER2 (A0485), Ki-67 (MIB1), bcl-2 (124), and p53 (DO7, all antibodies by Dako). Data were clustered with the aim of creating groups similar to those obtained by gene expression classification.

Results: 75% of all breast cancers could be clustered using this panel of 6 immunohistological tumor markers. 30.2% were clusted as Luminal A, 18.0% as Luminal B, 11.3% as erbB2-like, 5.4% as basal-like, and 10.1% as normal-breast like.

Conclusions: While phenotypic clustering is very well possible for hormone receptor positive tumor into Luminal A and B subgroups, the markers are not sufficient to predict basal phenotype. With the addition of basal cytokeratins to this panel, a good immunohistological classification should be possible.

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Basal- and non-basal phenotypes in triple-negative breast cancers

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Background: Triple negative breast cancers are characterized by lack of expression of oestrogen, and progesterone hormone receptors, and lack of HER2 overexpression. Frequently they are associated with a basal phenotype, but there is a distinct subgroup of “quadruple-negative” cancers which not basal-like, and are yet ill defined yet. Therefore, in the present study, we have analysed the expression of basal and other markers the triple negative breast cancers.

Materials and Methods: 158 triple-negative invasive breast carcinoma were selected from the archives and used for construction of tissue microarrays. A panel of immunohistochemical markers, which included ER, PgR, HER2, CK5/6, CK14, CK18, EGFR, p53, c-KIT, MKI-67, bcl-2, and p16 was used to further characterize these tumours.

Results: 102 tumours (66%) showed a basal phenotype by being positive for either CK5/6 or CK14 using a cutoff value of 10%. The non-basal triple-negative cancers differed from the carcinomas with a basal phenotype by having a lower proliferative rate ($p = 0.04$), and were less frequently CD117 positive (14% vs. 32%, $p = 0.01$) and less frequently overexpressed p16 (31% vs. 52%, $p = 0.01$). No differences were seen for bcl-2 (9% vs. 10%) and p53 overexpression (37% vs. 36%).