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BREAST CANCER

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Posters

Hassan E et al., Breast Can Curr Res 2017, 2:3(Suppl)
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Assessment of breast cancer occurrence among females at King Abdul Aziz Hospital, Al-Ahsa: A retrospective study from 2007-2014

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Breast cancer (BC) is the most common cancer among Saudi women, with an overall estimate of 26.6 cases per 100,000 in 2007, as reported by the WHO from 2012 to 2016. The study aimed to assess Breast Cancer occurrence among female patients in King Abdul Aziz Hospital -Al Ahsa eastern region. A retrospective cross-sectional descriptive design was utilized. The average age at the diagnosis was 51.9 ± 14.4, and ranged 40-60. BMI average was 31.1 ± 07.6. The most common comorbidities were diabetes, hypertension and heart disease (49.1%; 48.2% and 18.9%) respectively. Most BC cases were diagnosed with infiltrating ductal carcinoma (79.3%), Half of the cases had tumor size of 2-5cm (T2) and 39.4% with grade III. In 2007, most of the cases (80%) were positive (HER2) but it decreased to 27.3% in 2014. The common manifestation among cases was a mass in the breast (lump), pain and lymph node involvement. The first line of treatment that is used for those patients included mastectomy (79.6%), chemotherapy (67.9%), radiation (34.0%) and hormonal (15%). In conclusion, BC is still diagnosed in women younger than 50 years old than other developing country. Most of them had infiltrating ductal carcinoma and more than one third of cases has grade III. The most common comorbidities associated with BC were diabetes, hypertension and heart disease. BC awareness campaigns and resources are needed to early detect and screen BC cases to decrease the mortality and increasing the survival rate and to meet the future increase in BC.

Biography

Eman M.G. Hassan has completed her PhD from Faculty of Nursing (FON), Cairo University, Egypt in 2010. She has been working currently as assistant professor in College of Nursing, Al. Ahsa (CON-A), King Saud bin Abdul Aziz University for Health Sciences (KSAU-A), KSA since 2010. She was a chairperson of quality unit in CON-A for last 2 years

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Jana Slobodnikova et al., Breast Can Curr Res 2017, 2:3(Suppl)
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Radial scare- the comparison of ultrasound breast imaging with histopathology

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Aim: Compare the benefits of ultrasound, mammography, MR mammography and biopsy - for breast imaging in the diagnosis of a radial scar with histopathology.

Material & Method: The retrospective study of the histologic findings of 54 patients with radial scare or complex sclerosing lesion. Retrospective study from January 2003 to December 2015 was done. In all patients we performed clinical examination, mammography, ultrasound, magnet resonance and core cut biopsy. We compare results of ultrasound results with breast imaging and definitive histopathology.

Result: In all the 54 patients we compared clinical examinations, sonography and mammography of a MR imaging with histopathology. In all 39 patients in US imaging we described changes in architectonics structural distortion tissue, mass and in centrum, 10 lesions were found for scar. Only 5 lesions were in US atypically. With combine US, MG and biopsy was correctly diagnosed in 44 cases. The 10 cases were diagnosed after surgical treatment of a histopathology.

Conclusion: Typical radial scar is a benign breast lesion, which increased clinical significance. Radial scar is frequently associated with atypia and/or the breast malignancy. We cannot currently reliably exclude malignancy in radial scar by breast imaging, excision biopsy (core cut biopsy, vacuum assistant biopsy) is recommended. US is very important image modality for correct diagnosis of radial scare.

Biography

Jana Slobodnikova has done her MD from Prague Charles University. She has completed CSc/PhD from Institus of experimental Oncology Slovac Scientic Academy. She also worked as an Ass. Prof. Trnaviensis University. She has published more than 90 scientific papers, from then 25 papers in reputed journals and has been serving as an Editorial Board Member of repute. She has published 3 monographs. She is President of the section of breast imaging of Slovak Radiologic Society and Vice President of the Slovak Society of Ultrasound in Medicine

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Mathieu Vernier, Breast Can Curr Res 2017, 2:3(Suppl)
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Inhibition of the orphan nuclear receptor estrogen related receptor alpha sensitizes breast cancer cells to DNMT inhibitors

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Alterations in DNA methylation are implicated in the acquisition of malignant phenotype, and the use of epigenetic drugs is a promising strategy for anti-cancer therapy. In breast cancer, cell metabolism is tightly regulated by the oncogenic nuclear receptor estrogen-related receptor alpha (ERRa) and we wondered whether ERRa regulates SAM levels and DNA methylation. A gene signature designed to assess ERRa activity reveals that patients with high ERRa activity have a shorter free-disease survival. Interestingly, expression of the principal DNA methyltransferase DNMT1 follows the expression profile of ERRa gene signature. Further analysis of chromatin immunoprecipitation experiments followed by DNA sequencing (ChIP-seq) of ERRa conducted in breast cancer cell lines showed that ERRa is located on the promoter of DNMT1 and many genes implicated in one carbon metabolism. Inhibition of ERRa reduced DNMT1 expression at the mRNA and protein levels and induced changes in SAM levels. Therefore, treatment of breast cancer cells with the ERRa inhibitor C29 highly sensitized these cells to the DNMTi. Surprisingly, inhibition of DNMT1 reduced protein levels of ERRa, unraveling the existence of a feedback loop. Further investigations on mouse models will be conducted to validate these results in vivo. We propose that patients with high ERRa activity would respond well to a combined treatment of ERRa and DNMT inhibitors.

Biography

Mathieu Vernier has completed his PhD from Montréal University and and is currently achieving his postdoctoral studies from McGill University. He has authored more than 15 publication in the area of Molecular Biology and Cancer research during his doctoral studies

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Ruth McCrea, Breast Can Curr Res 2017, 2:3(Suppl)
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Exploring the effects of an exercise programme on women with breast cancer

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Background: Emerging evidence suggests that regular exercise plays an important role in improving physical function and quality of life following a breast cancer diagnosis. Evidence also suggests it can reduce the risk of recurrence. Despite these benefits, research has shown that women with breast cancer are known to reduce their activity during treatment and afterwards. More research is required to explore what type of interventions may help these women become more active.

Design & Methods: The breast unit charity, at St Margaret's Hospital, Epping, funded a qualitative study to explore if running exercise classes in the hospital gym would aid or initiate return to exercise. The classes ran weekly, for 6 weeks, led by a fitness instructor, trained to CanRehab level 4 to ensure she had the requisite knowledge and expertise. 8 participants consented to attend these sessions. They were interviewed prior to and after the classes were completed which were audio taped and transcribed verbatim to ensure accuracy.

Results: The exercise sessions had positive effects on all but one participant who did not enjoy the aerobic element. The main study findings suggested that exercising with women in the same boat, with a specially trained instructor and being informed of the benefits of exercise could help women to become more active.

Conclusion: 56 patients have now attended classes over the last year due to team referrals and continued funding. An on-going service evaluation has highlighted 70% wish these classes continue and now a further class is running in the community.

Biography

Ruth McCrea trained as a RGN at The Royal London Hospital and is the lead Research Nurse in the breast unit at St Margaret's Hospital, Epping, which runs numerous trials in all aspects of breast cancer. She is a Member of one of the trials management groups. She has completed her MSc at The Royal Marsden and St George's University of London and her dissertation involved the setting up and exploring the effects of this exercise programme. Due to the positive outcomes and further funding, these sessions are now being offered to all patients who attend the breast unit.

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Notes:

Shintaro Asai, Breast Can Curr Res 2017, 2:3(Suppl)
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Problems of mammary prosthesis inserted for a long period

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Objective: Recently, mammary prosthesis for the cosmetic purposes or breast reconstruction after breast cancer tends to increase. However, a variety of complications from earlier period due to mammary prosthesis has also been reported. But there are few reports of mammary prosthesis complications after a lapse of more than 10 years after operation.

Materials & Methods: This time, I have experienced the 5 patients who were operated after a long period (average 22.6 years), and were also required the extraction of mammary prosthesis.

Discussion: In addition to mammary augmentation for cosmetic purposes, mammary prosthesis after breast cancer resection has became insurance adaptation in Japan. Mammaly augmentation by mammary prosthesis can be considered to increase in the future. I will report the task and counter measure the mammary prosthesis, in the discussion.

Biography

Shintaro Asai has a passion for plastic surgery and aesthetic surgery. He has experienced in research, evaluation, teaching and administration both in hospital and education institutions for many years. Now, His working at Nagoya Kyoritsu Hospital, Nagoya, Japan.

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e-Poster

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An analysis of the use of neo-adjuvant chemotherapy with trastuzumab for patients with HER-2 positive breast cancer

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Use of anti-HER-2 therapy with chemotherapy in the neoadjuvant setting improves pathological complete response (PCR) rate. Patients with HER2-overexpressing tumors who achieve PCR had better event-free survival and overall survival. The proportion of patients achieving PCR with addition of neoadjuvant trastuzumab is 22.6-65.2%. Dual anti-HER-2 therapy has been recommended in selected high risk cases. This study primary aim is to determine PCR rate in HER-2 positive breast cancer patients who have received neoadjuvant chemotherapy and trastuzumab in the heart of England Foundation Trust, and to identify their tumor characteristics. Secondary aims are to establish proportion of patients who had breast conserving surgery and those who developed recurrence or metastases. Data was collected retrospectively to include cases from January 2011 to 2016 using the hospital electronic system. 18 patients were identified who had HER-2 positive invasive ductal carcinoma and received neoadjuvant fluorouracil, epirubicin and cyclophosphamide followed by docetacel and trastuzumab 16(89%) had a pathological response and 10(56%) had a complete pathological response. Among those who achieved PCR, 50% were hormonal receptor negative and 70% had graded 3 tumors and positive lymph nodes. Overall, 44% of patients had breast conserving surgery. One patient developed local recurrence and two patients had metastases. Our data showed that the rate of PCR achieved in our unit is comparable with other studies. Patients with more aggressive tumors appeared to achieve a better response however a larger sample size is needed to further strengthen this association.

Biography

Ik Shin Chin is a Specialty Registrar Trainee in medical oncology. She is currently working with the breast care team in the Heart of England NHS Foundation Trust in Birmingham, West Midlands.

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Accepted Abstracts

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Wnt-DP103-GSK3β cascade promotes Wnt/β-catenin signaling in parental and stem cells from triple negative breast cancer

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Despite recent advances in breast cancer therapeutics, mortality of highly metastatic triple negative breast cancer (TNBC) subtype remains high; due to their lack of hormone receptors expression for targeted therapy. Therefore, there is a pressing need to identify new prognostic markers and therapeutic targets for this group of breast cancers. Aberrant activation of Wnt/β-catenin signaling has been associated with breast cancers; where 40% of total breast cancers have elevated β-catenin levels and/or Wnt activity. Herein, we identify DEAD-box RNA helicase DP103 as a novel driver of Wnt/β-catenin pathway in TNBC. The link between DP103 and Wnt/beta-catenin signaling was further validated using in vivo Zebrafish models, where disruption in DDX20 gene splicing mechanisms resulted in severe early embryonic developmental defects which phenocopies loss of Wnt/beta-catenin signaling during gastrulation. Interestingly, we also show DP103 drives breast cancer stem cell (CSC) formation, a process regulated by the Wnt/beta-catenin pathway. Depletion of DP103 led to a marked reduction in the percentage of CSC-enriched mammospheres with reduced tumor-initiating ability. Mechanistically, we show DP103's role in driving Wnt/beta-catenin pathway is independent of casein kinase I activity but highly dependent on GSK3β activity. More interestingly, from molecular docking data, we found DP103 protein has to be phosphorylated at threonine residue 552, when it interacts with GSK3β. Surprisingly, induction of Wnt/β-catenin signaling also significantly increased DP103 expression, indicating a possible positive feedback loop. Collectively, our data suggest a novel regulatory role of DP103 in the Wnt/β-catenin signaling pathway in parental and CSC derived TNBC.

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Talking to children and young people about hereditary breast cancer

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Many families with a family history of breast or ovarian cancer will request genetic testing to ascertain whether family members carry the gene mutation. The gene test results will indicate whether women need to undergo additional screening measures and receive prophylactic treatments to reduce their risk of developing cancer. Whilst many families welcome the opportunity to receive this additional surveillance a major concern that continues is when and how parents should talk to their children about the cancer and hereditary risks. We carried out semi-structured qualitative interviews with 11 families, which included parents, children (7-11years) and young people (12-18 years) to learn more about families' experiences about managing these sensitive conversations and the effect upon their family functioning and coping with the risk information. The interview transcripts were coded and thematically analyzed. Four themes emerged from the data on family communication, perception of cancer risk, managing risk and the impact of genetic risk upon children and young people's decision-making. Our findings showed that parents were worried for their children but only discussed a limited amount of information about the cancer risk and particularly about the psychological effects of prophylactic measures. Children and young people often did not realize implications of prophylactic procedures, especially bilateral mastectomy and breast reconstruction. With contemporary Western society's acceptance of cosmetic surgery, many children and young people focused predominantly on the perceived positive benefits without realizing more fully the physical and psychological consequences of managing the risk information and the outcomes of surgery.

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Contrast enhanced spectral mammography in the sympatomatic setting: Initial findings from a single UK institution

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Contrast enhanced spectral mammography (CESM) is a novel technique in breast imaging in which mammographic images are acquired before and after the intravenous injection of iodinated contrast. The use of standard mammography is limited in dense breasts and there is increasing evidence demonstrating the added value of CESM in a symptomatic setting. The aim of this presentation to share our experience of CESM in charactersing breast lesions in symptomatic patients at our institution.

The main contents of the presentation will be:

1. Introduction to CESM technology – why and how is it done at our institution?
2. Results from our 2-year restrospective analysis of CESM in characterising breast lesions which included sensitity, specificity, PPV and NPV for detecting cancers. Comparison with MRI and final surgical histology will also be included.
3. A selection of case studies including false positives and false negatives

Conclusion: The future role of CESM.

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Impact of moderate intensity aerobic exercise on chemotherapy-induced anemia in elderly women with breast cancer: A randomized controlled clinical trial

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Exercises are often recommended for patients suffering from anemia to improve physical conditioning and hematologic parameters. Hence, the present study aimed to investigate the impact of moderate intensity aerobic exercise on chemotherapy-induced anemia. 30 elderly women with breast cancer underwent chemotherapy and were randomly assigned into two equal groups, Group A received aerobic exercise for 25-40 minutes at 50-70% of the maximum heart rate, 3 times/week for 12 weeks in addition to usual daily living activities, medication and nutritional support. Group B who did not train served as controls. Hemoglobin (Hb), and red blood cell count (RBCs) were evaluated pre-treatment and after 12 weeks of training. There were significant declines of both Hb ($t=16.30$; $P<0.001$) and RBCs ($t=10.38$; $P<0.001$) in group B relative to group A. Regarding group A, Hb increased from 11.52±0.62 to 12.10±0.59 g/dL with a 5.03% change, while RBCs increased from 4.24±0.37 to 4.49±0.42 million cells/μL with a 5.89% change. Between-group differences were noteworthy regarding Hb ($t=-5.34$; $P<0.001$) and RBCs ($t=-5.314$; $P<0.001$). The results indicate that regular participation in moderate intensity aerobic exercise can enhance chemotherapy-induced anemia.

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Value of biannual DCE-MRI in surveillance of high risk women: Is it worthy?

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Purpose: The purpose of this study is to evaluate the diagnostic value of biannual dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) regarding the early detection of breast cancer in women at elevated risk.

Materials and Methods: A retrospective review was performed of the records of 232 asymptomatic women at elevated risk for breast cancer (mean age at entry: 44 years; range: 22-73 years). A total of 1440 biannual DCE-MRI rounds and 802 annual screening mammography rounds from 2002 to 2014 were reviewed. All lesions were detected as abnormal enhancing findings on a dynamic contrast enhanced MRI and subsequently biopsied. Pathology findings were then correlated with imaging to ensure concordance.

Results: A total of 33 biopsies were performed on 31 high risk women (PPV2: 21%). As a result, 7 cancers (21%) and 26 benign lesions (79%) were detected (PPV3: 21%). Of the detected cancers (2 DCIS and 5 IDC), 0 were axillary node positive. Mean size of detected invasive cancer was 0.7 cm (range: 0.4–1.1 cm) and the most common imaging appearance was an enhancing mass (86%). Of these cancers, 5 (71%) were detected in patients with a personal history of cancer and 6 (86%) were in non-baseline examinations. All 7 cancers were detected on DCE-MRI, 4 of which were seen only on DCE-MRI (56%).

Conclusions: Biannual screening DCE-MRI can serve as an effective surveillance tool in high-risk women, particularly for the detection of small, node-negative breast cancers. Biannual screening DCE-MRI may allow for the detection of smaller cancers than with annual screening DCE-MRI.

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Inhibition of breast cancer by resveratrol and resveratrol analogs

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Most of the currently available drugs to treat breast cancer (BC) have major limitations in long-term use because of significant toxicities or adverse effects associated with these drugs. Published studies have established that resveratrol (Res), possesses antioxidant, anti-inflammatory and anticancer activities. Unfortunately, however, the available evidence supports the conclusion that its potency in preventing or treating BC is relatively modest at best. We hypothesize that this problem can be successfully addressed through synthesis of Res analogs with appropriate structural modifications. We have synthesized a series of novel compounds that resemble the basic Res skeleton but contain some structural modifications with different pharmacophoric groups. We evaluated these compounds for their cytotoxicities against several BC cell lines. We demonstrate that one of the synthesized compounds 4-(E) {(p-tolylimino)-methylbenzene-1,2-diol} (TIMBD) has significantly higher potency than Res in inhibiting the growth of all BC cell lines that we tested. Moreover, TIMBD did not have any detectable detrimental effect on the growth of normal (non-neoplastic) human breast cells and other cell types of the brain. Additionally, increased oxidative stress has been suggested to contribute to development of breast tumors and many other diseases. Our preliminary results suggest that TIMBD also functions to decrease levels of oxidative stress, induce mRNA and protein expression levels of antioxidant defense genes such as NQO1, SOD3 and Nrf2 in normal (non-neoplastic) breast cell lines as well as in human SVGA astrocytes but not in BC cells. Our results thus suggest that TIMBD is not only cytotoxic towards BC cells but can also help to protect normal cells against increased oxidative burden. Thus, chemotherapeutic agents that have the potential of specifically killing, or inhibiting the growth of, BC cells with relatively minimal toxicity towards normal cells, would be expected to have a significant therapeutic advantage in selectively targeting BCs.

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Evolution of a comprehensive, multidisciplinary screening program to identify patients at high risk for breast cancer: A revised pilot study

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Introduction: Screening for patients at high risk for breast cancer has become a major part of any breast health program. Unfortunately, patient compliance is generally low and involvement of physicians and potential patients is difficult to obtain.

Methods: In April, 2016, a comprehensive, multi-disciplinary high risk screening program was instituted at a large community health system. Over the first three months, over 4000 screening mammograms were done and 432 patients identified as eligible for high risk screening. Of these, 114 were eligible for genetic counseling and testing. Unfortunately, a very high percentage of patients either refused or did not show for appointments. In July, 2016, therefore, a revamping of the program was undertaken with the goal of improving those numbers. A widespread educational effort was instituted, and a Breast Navigator was utilized more directly in the process.

Results: A second 3-month pilot study (PS-B) was begun in August, 2016, and the results compared to the 3-month pilot prior to re-organization (PS-A). Total screening mammograms performed, percentage of patients eligible for high risk screening, and percentage of those eligible for genetic testing/counseling were not significantly different between PS-A and PS-B. Significantly fewer patients refused counseling in PS-B, however-20.7% vs. 35% in PS-A. There were also significantly fewer no-shows: 3.3% in PS-B vs. 16.2% in PS-A.

Conclusions: Success in a high-risk screening program is dependent upon both patient information, patient and physician acceptance, and continuous and effective communication. This is a dynamic process that requires dedicated resources and personnel to be effective.

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Clinical features of patients with breast cancer related lymphedema and effects on hand muscle strength

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Objectives: To investigate the clinical characteristics of lymphedema patients with breast cancer and assess the effect of lymphedema on hand muscle strength

Methods: We retrospectively reviewed the medical records of 18 patients who first visited to our department and were diagnosed with lymphedema January 2016 to February 2017 at outpatient clinic. The demographic data, beck depression inventory (BDI), montreal cognitive assessment (MOCA), BMI (body mass index) swelling and handgrip strength were recorded. The arm circumference measurements were taken of wrist, 5 centimeter below the elbow, and 10 centimeter above the elbow joint. Jamar dynamometer was used to determine hand grip strength.

Results: Among the 18 patients, the mean age was 55.0±12.1. The mean BDI score was 19.7±5.5. In addition, average MOCA score was 23.3±5.6 and BMI score was 23.7±1.9. Circumference of lymphedema side was higher than other side at all levels. The hand grip strength of lymphedema side was lower than the other side strength ($p=0.015$) and significantly lower than normal group ($p=0.029$, Table 1). A positive correlation was noted between hand grip strength difference and circumference difference ($P<0.05$, Table 2).

Conclusions: The degree of edema is related to the strength of the hand with breast cancer related lymphedema patients. Also, mild depressive pattern and overweight may appear in patients with lymphedema. These findings will help us to understand breast cancer rehabilitation and more comprehensive research is needed in the future.

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Contralateral prophylactic mastectomy with reconstruction increases health care utilization and cost

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Background: Rates of contralateral prophylactic mastectomy in women with unilateral breast cancer continue to rise, especially in women undergoing immediate breast reconstruction (IBR).

Methods: We utilized administrative claims data from a large U.S. commercial insurance database (OptumLabs) to identify women age 18+ years who underwent IBR 1/2004-12/2013. We compared 2-year total costs of care and unadjusted utilization rates between unilateral mastectomy (UM) and bilateral mastectomy (BM) for implant-based and autologous reconstruction. Comparisons were tested using t-test and differences in cost were estimated with Wilcoxon rank sum test.

Results: 11,728 women undergoing mastectomy with IBR were identified; 7,693 with implant reconstruction (2,090, 27% UM and 5,603, 73% BM) and 4,035 with autologous reconstruction (1,754, 43% UM and 2,281, 57% BM). Mean hospital length of stay at initial surgery and overall rate of office visits was similar between BM+IBR and UM+IBR, however rate of A&E visits was higher for BM+IBR (34.2 per 100 women vs. 30.2, p<0.0001). For implant reconstruction total 2-year cost of care was higher for BM+IBR than UM+IBR for commercial insurance ($106,469 vs. $96,689, p<0.001) however it was not significantly different for medicare advantage. For autologous reconstruction, total medicare advantage 2-year cost of care was higher for BM+IBR ($57,602 vs $37,713, p=0.027) with even greater differences seen in commercial insurance.

Conclusion: BM+IBR (autologous or implant) was associated with increased A and E visits and higher total cost of care over 2-years compared to UM+IBR. Patients considering contralateral prophylactic mastectomy should be counseled on the additional risks and costs associated with BM+IBR.

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GT198 and Her2 double positivity as an improved therapeutic marker for herceptin treatment in human breast cancer

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Breast cancer is a lethal cancer in women. It is urgent to identify new therapeutic biomarkers to facilitate the treatment. Therapeutic drug Herceptin (trastuzumab) is effective in Her2-positive breast cancer treatment, however, there is inconsistency to distinguish responders versus non-responders using Her2 as a sole biomarker. The human GT198 gene is a breast and ovarian cancer gene at chromosome 17q12, 2.9 Mb proximal from the ERBB2 gene encoding Her2. Both germline mutations and high frequency somatic mutations in *GT198* are present in breast and ovarian cancer. In breast and ovarian tumors, somatic mutations are present in tumor stromal stem cells. Gene copy number increase of *GT198* has also been found in breast cancer. Here we find that Her2 and *GT198* proteins are co-expressed in breast tumor stromal cells carrying *GT198* mutations, suggesting that Herceptin may in fact also target *GT198*-positive tumor stromal cells. Her2 gene amplicons generally encompass large genomic regions, thus the two adjacent genes may co-amplify and result in coexpression. Our finding suggests that *GT198*/Her2 double positivity is potentially a more specific therapeutic marker for Herceptin. In particular, positive tumor stroma, in addition to tumor, deserves more attention in clinical decisions. Since herceptin is extensively used in the treatment of breast cancer and *GT198* is a causative breast cancer gene, this study provides insights into novel mechanisms associated with herceptin efficacy and reveals new biomarker using *GT198* for improved targeted therapy.

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Recurrent phyllodes tumor – A clinical perspective

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Phyllodes tumour of the breast is a rare fibroepithelial neoplasm that are known to recur locally in up to 19% of patients. Exact cause is still an enigma. Clinical symptoms are extremely similar to the more common fibroadenoma and are therefore often locally excised without any gross surgical margins. Accurate preoperative pathological diagnosis allows correct surgical planning and avoidance of recurrence and subsequent surgery. In this report, we present a case of benign phyllodes tumour with a presentation of recurrence. 56 years female with a history of breast swelling size of 4cm since 3 years attended as outpatient. No lymphadenopathy was noted. A history of swelling at the same location, 5 years back which was surgically removed has been reported. FNAC was suggestive of fibroadenoma. Histopathologically the tumour was diagnosed to be phyllodes tumour. Though there is no previous report, it suggests recurrent phyllodes tumor due to their tendency to recurrence and inadequate local excision surgically. Immunohistochemistry with the markers CD34 (+), CD117 (-) and with low proliferative index of Ki67 confirms the diagnosis. Recurrent tumours are histologically similar to that of primary tumours. Core needle biopsy has been reported to be more accurate than FNAC. Our study suggests that, preoperative diagnosis and efficient surgical management are very important to avoid recurrence of phyllodes tumours.

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Role of post translational modifications in breast cancer

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Breast cancer is the most common cancer in women worldwide, and resistance to the current therapeutics, often concurrently, is an increasing clinical challenge. Glycosylation of proteins is one of the most important post translational modifications. It is widely known that aberrant glycosylation has been implicated in many different diseases due to changes associated with biological function and protein folding. Alterations in cell surface glycosylation, can promote invasive behavior of tumor cells that ultimately lead to the progression of cancer. In breast cancer, there is increasing evidence pertaining to the role of glycosylation in tumor formation and metastasis. In the present study an attempt has been made to study the disease associated sialoglycoproteins in breast cancer by using bioinformatics tools. The sequence will be retrieved from uniprot database. A database in the form of a word document was made by collection of FASTA sequences of breast cancer gene sequence. Glycosylation was studied using yinOyang tool on expasy, followed by involvement of differentially expressed genes in important molecular and signaling casades using KEGG, DAVID and ingenuity databases. The number of residues predicted O-glc NAc threshold -2 or more was detected and recorded for individual sequence. We found that the there is a significant change in the expression profiling of glycosylation patterns of various proteins associated with triple negative breast cancer. Differential aberrant glycosylated proteins in breast cancer cells with respect to non-neoplastic cells are an important factor for the overall progression and development of cancer.

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Glucose regulated protein (GRP-78)-mediated selective phosphorylation of Akt on threonine 308 sensitizes breast cancer cells to tamoxifen-induced cytotoxicity.

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Breast cancer is the most prevalent cancer in women. Tamoxifen (TAM) has been used for several years as an effective drug for treating estrogen receptor positive breast tumors. However, resistance to TAM is a major challenge in treatment of breast cancer. Accumulating evidence has highlighted the role of Glucose-regulated protein (GRP)-78, the master regulator of the unfolded protein response, in chemoresistance. The present study aimed to decipher the function of GRP78 during response to TAM in breast cancer cells. Among a panel of drugs -paclitaxel, doxorubicin, 5-fluorouracil, UCN-01 and tamoxifen, only TAM induced apoptosis and up-regulated the expression of GRP78 in MCF-7 and MDA-MB-231 cell lines. Inhibition of GRP78 augmented apoptosis and overexpression rendered the cells resistant suggesting a decisive role for GRP78 in TAM-mediated cytotoxicity. Mechanistically, TAM selectively unregulated phosphorylation of Akt on Thr308 but not on Ser473, and silencing of GRP78 resulted in inhibition of Akt (Thr308) phosphorylation. GRP78 inhibition prevented TAM-induced phosphorylation of GSK3β, a downstream substrate of Akt implicating a role for GRP78 in TAM-induced Akt activation. Additionally, our study demonstrated a physical association of Akt and GRP78 that may be decisive for cell survival. The present study identifies a crucial role for GRP78 and Akt-mediated survival mechanism during TAM-induced response in breast cancer cells. The findings provide evidence for the protective function of GRP78 in stressed cells to promote drug resistance and suggest that a combination of compounds targeting GRP78 and anticancer drugs like TAM would be beneficial to overcome therapy resistance.

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A series study on brain metastasis for breast cancer

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Brain metastasis is the principle cause of death for breast cancer, we have conducted a series of studies on the occurrence, development, and treatment of breast cancer brain metastasis. Firstly, we analyze the clinical characteristics and prognostic factors of breast cancer patients with brain metastases, and found that WBRT+SRS is better than WBRT alone in multiple brain metastases, SRS alone can replace WBRT+SRS used in patients with less than three brain metastases. We also constructed a nomogram for predicting 1st and 2nd year overall survival, which exhibited good accuracy in predicting overall survival. Secondly, we investigated the risk and relapse of perihippocampal (PH) metastases in breast cancer, and found that hippocampal metastases were identified in 1.2% of metastases and 4.1% of patients. pH lesions comprised 3.5% of lesions in 11.1% of patients. The risks of PH metastasis recurrence were 4.6% for WBRT and 6.8% for sub-therapeutic irradiation in the pH region. Thirdly, we invested the characteristics of cystic BM in a large cohort of breast cancer patients and found patients with cystic metastasis were characterized by a larger metastasis volume, a shorter progression-free survival (PFS) following their first treatment for BM, and poor overall survival after BM ($p<0.05$). This study shows that cystic BM from breast cancer, a special morphological type of BM, had worse prognosis than the more commonly observed solid BM. Fourthly, we revealed that reirradiation is an effective and a safe treatment for patients with brain metastases from breast cancer. Patients with a high KPS score, stable extracranial metastasis and good response to reirradiation might be benefit from reirradiation, whereas patients with peritumoral edema, cystic brain metastasis and a low KPS score might not be appropriate candidates for reirradiation.

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Tentative title of the talk: Epigenetic regulation in breast cancer and combination therapy

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Traditional therapies do not kill cancer progenitor cells and drug-resistant cancer cells, causing cancer relapse. Interestingly, combination therapy, including epigenetic drugs, was effective against breast and ovarian cancers causing more than additive growth inhibition in various types of breast and ovarian cancer cells. Our recent analytical study suggests that breast and ovarian cancers possibly have similar epigenetic origin. Other studies have shown that combination therapy with epigenetic drugs reduced cancer relapse, sensitized drug resistant cancer cells, and killed cancer stem cells. These findings led us to hypothesize that initiation of cancer progenitor cell formation from predisposed cells requires an epigenetic switch. Further development of cancer involves mutations. This hypothesis contradicts current paradigm of carcinogenesis. CpG residue methylation in the upstream regions of genes is one of the epigenetic regulations involved in silencing of tumor suppressor genes in cancer cells. In addition, histone modifications, such as H3K4me, and H3K27me3, and other histone modifications regulate gene expression in concert with alterations in DNA methylation. Our system biology analysis revealed that DNA methyl transferase1 (DNMT1), the enzyme which maintains CpG residue methylation is allosterically activated in cancer cells. H3k9me3 recruits DNMT1 at the site of CpG methylation. It is possible that histone modification and CpG methylation work in a concert to regulate differential gene expression in carcinogenesis.

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First results of a pre-planned interim analysis of a national multicenter patient reported outcome study (PRO-Bra) in breast reconstruction following mastectomy with titaniferously coated polypropylene mesh (TiloopBra)

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Introduction: In the majority of interdisciplinary breast centers of Germany implant based, mesh-supported operations constitute a total of approximately 50-60% of reconstructive techniques. The BreastQ is the most valid and reliable measurement of quality of life aspects in important domains used in clinical routine.

Material & Method: Because the patient reported outcome is the most relevant factor reflecting the overall satisfaction from a patient perspective a prospective surveillance study with BreastQ-scales at 12 months as primary endpoint was conducted (2013) and ended 7/2016 with full recruitment (n=267). A pre-planned analysis of the first 60 pts with completion of the BreastQ after 6 months was done.

Results: Almost all surgeries were primary reconstructions (96.6%) and nipple-skin-sparing mastectomies (97.1%). The most frequent incision was inframammary (n=115), followed by T-shaped (n=45). The average of the pts was 50 y (19-77), BMI was 22 (17-33), 77.3% were non-smokers. Percentage of neoadjuvant chemotherapy was 23% of prior radiotherapy was 12%. Radiotherapy showed no significant influence of the BreastQ. Severe events occurred in 46 cases. The most frequent complications were necrosis (n=12), hematoma (n=12) and 9 pts were dropped out. The mean score of BreastQ was equal pre and postoperative after 6 months (67+/-16 to 65+/-15) satisfaction with breast from 67+/-22 to 61 +/-14; psycho-social well-being from 71+/-17 to 73+/-18, sexual well-being from 62+/-17 to 60+/-19, satisfaction with outcome was 75+/-18 and satisfaction with surgeon 90+/-15. 88.3% were very satisfied, 10.0% somewhat satisfied, only 1.7% somewhat dissatisfied and 0% very dissatisfied.

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Search for new genetic mutations for breast cancer among high risk groups in Jordanian population

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Introduction: Breast cancer is the most common cancer in females. Worldwide more than 1 million new cases are diagnosed each year and nearly 600,000 women die from breast cancer each year. Breast cancer contributes to 37.4% of female cancers in Jordan and the second cause of death among women after ischemic heart disease. 22.8% of mortality from cancer among women was due to breast cancer with 211 reported deaths. Hereditary predisposition is estimated to cause about 7% of all breast cancers. Of all familial breast cancers, about 50% of cases are due to mutations in the BRCA1 and BRCA2 genes and are associated with early-onset breast cancer. The above two genes were identified in Ashkenazi Jewish. Studying other close populations could help identifications of new genes. A study conducted in Jordan showed a high consanguineous mating rate of 63.7%. Therefore, in such country with a very high consanguinity rate, genetic studies could identify new mutations or new genes related to breast cancer.

Aim & Methodology: In this cross-sectional study, we aimed to evaluate the potential contribution and the frequency of mutations in the BCRA1, BCRA2 gene in selected Jordanian patients with breast and ovarian cancers and in their first degree family members. We also aimed to search for new mutations in selected Jordanian patients with breast or/and ovarian cancer. We used the NICE guidelines for strong family history of breast/ovarian cancers in the selection criteria.

Results: 205 patients and 200 controls were included in the study. The mean age of study participants was 44. 195 patients had breast cancer and 10 cases had ovarian cancer at primary site. 15 patients had bilateral cancer. Results showed that there were 35 patients with confirmed mutations for breast cancer and 41 patients with confirmed or possible mutations with prevalence of 17% for the first group and 20% for the second group. Regarding site of mutation, 7% had confirmed mutations in BRCA1 gene and 12% had confirmed mutations in BRCA2 gene. Six patients had possible new mutations in BRCA2 gene and needs to be studied further among families of the patients.

Discussion & Recommendations: There is an urgent need for a national program for familial cancer referral and management system. This could be achieved through establishing a familial breast and ovarian cancers service in the first stage and expanding this in the future for all cancers. Patients and family members should be seen for genetic testing, counseling and management. This will lead to reducing mortality and morbidity from breast cancer and could save millions from treatment of advanced breast cancer or ovarian cancer for these high risk groups.

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Controversies in screening breast cancer

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There is established consensus in breast health community that mammography is the mainstay imaging examination for screening breast cancer. However, there are varied national recommendations among stakeholders and major institutions in the topic of breast cancer screening. Lack of consensus in screening criteria includes risk stratification, age to initiate screening and the interval of screening. The differences in practice guidelines are mainly due to variation in design and interpretation of screening trials over the past decades. As debates for and against the use of screening mammography continue to escalate, both providers and patients are often confused and wrongly perceive the recommendations as directives. The purpose of this presentation is to review the current guidelines, analyze the reason for the controversies in screening mammography and shine light on the upcoming trends of future screening guidelines.

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