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2nd World Congress on

# Breast Cancer

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# Cancer Science and Therapy

September 16-17, 2019 | Edinburgh, Scotland

## Poster

30 YEARS OF EXCELLENCE IN MEDICAL PUBLISHING

# Risk factors effect on survival of breast cancer females after recurrence

**Madiha Liaqat**
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**Statement of the Problem**: Women having HER2 positive have a high low survival rate. With all the risk factors including family history, obesity, late or no pregnancy and age, biomarkers such as ER, PR and Her2.neu consider to make prediction of women's survival. Usually recurrence occurs, previous researches have shown that after recurrence chances of survival decline. But till now no research has shown overall solid results of all the risk factors on survival by including biomarkers. The purpose of this study is to make solid conclusion after applying statistical methods on data collected from the last five years' cases of breast cancer, parameters are all the risk factors, biomarkers and targeted therapy. The main motivation behind this work is application of modeling to breast cancer data, in order to investigate the abilities of potential biomarkers of breast cancer with other parameters to predict patients' survival.

**Methodology & Theoretical Orientation**: It is a retrospective study, in this study patients' followed for 7 years. Sample size of study is 580. Graphs use to show relationship between different variables. Survival analysis tools and techniques use to depict patients' survival based on different variables.

**Conclusion & Significance**: Many variables have significant effect on survival. But many others like ER has not significant effect. Middle ages women have higher probability of death, even after treatment. Recurrence also have significant effect.

## Biography

Madiha Liaqat is a biostatistician doing PhD in Statistics from university of the Punjab, Lahore, Pakistan. She is working on breast cancer, and are developing new statistical tools and techniques which can be used to precisely predict patient's recurrence and survival.

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# Five day Accelerated Partial Breast Irradiation (APBI) using Stereotactic Body Radiation Therapy (SBRT) in stage 0-II breast cancer: A preliminary report of 69 cases

**Valerie Gorman**
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**Background**: Randomized trials in Stage 0-II breast cancer with 10 year follow-up have proven that Accelerated Partial Breast Irradiation (APBI) given via radiation implant in 5 days is equivalent to Whole Breast Radiation Therapy (WBRT) in 6 weeks in regard to tumor local recurrence (LR). However, implants are invasive and complications, including infection and soft tissue necrosis requiring possible mastectomy have been significant. Recently APBI using non-invasive Intensity Modulated Radiation Therapy (IMRT) in 5 days was shown to be equivalent to WBRT in 6 weeks with 5 year follow-up, with respect to LR [4]. APBI IMRT was superior in regard to side effects, and cosmesis.

**Objectives**: In the randomized clinical trial of APBI IMRT, the Clinical Target Volume (CTV) was defined by the injection of individual fiducial markers bordering the surgical cavity. We have used the simpler less labor intensive Biozorb fiducial system to localize the CTV for SBRT.

**Materials and Methods**: Between 2017 and 2019, 69 patients underwent SBRT targeted to Biozorb defined CTV. Eligible patients were older than age 40, had tumor sizes < 3 cm, negative surgical margins, and negative node dissections. SBRT dose was 30 Gy given in 5 fractions. The Planning Target Volume (PTV) ranged from 27 to 355 cc with a median of 80 cc. PTV = CTV + 1-2 cm.

**Results**: Follow-up ranged from 1-18 months with a median of 9 months. LR has been 0% (0/69). There were no skin reactions. Cosmetic results were rated excellent in 100% (69/69) of cases.

**Conclusions**: Non-invasive APBI with SBRT given over 5 days targeted to Biozorb has resulted in LR, complications, and cosmetic results which compare favorably to invasive APBI given via implant. At last follow-up, there have been no LR, skin reactions, or complications. Cosmesis has been excellent in 100% of patients.

## Biography

Valerie Gorman, MD, FACS is a breast surgeon who specializes in surgical oncology and surgical diseases of the breast. She is board certified by the American Board of Surgery and is a fellow of the American College of Surgeons. Gorman served as Chief of Oncology at Baylor Scott & White Medical Center - Waxahachie for eight years and currently serves there as Chief of Surgery and Medical Director of Surgical Services. Gorman has been in private practice in Texas since 2004.

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# Accepted Abstracts

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# Intraoperative radiation therapy in the complex treatment of localized breast cancer: Own experience

**Zandaryan A**
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**Introduction**: The combination therapy of localized breast cancer (LBC) with external beam radiation therapy (EBRT) is accompanied by a number of particular problems and needed more time to treat patients. Goals, to demonstrate that intraoperative radiotherapy (IORT) would be modest compared to the external beam radiation therapy (EBRT).

**Methods**: We performed retrospective analysis of short-term outcomes of 100 breast cancer patients, who underwent breast-conserving surgery(BS) combined with radiotherapy (RT) (2017). patients are in the under 62±3, the tumor size was 2.5 cm with luminal biological subtype of tumor. The Intraoperative radiotherapy (IORT) was carried out using «INTRABEAM PRS 500», the external beam radiation therapy (EBRT) was conducted with the help of «Electra Synergy».

**Results**: The patients were divided into 2 groups. The first group consists of 42 breast cancer patients with stage I and 8 breast cancer patients with stage II. The BS was combined with the IORT on «INTRABEAM PRS500». A single dose in first group ranged from 12 to 20 gy. The overall time of BS + IORT was 70-120 minutes. At the first group the post radiotherapy skin is not revealed. The average time of the treatment is approximately 35±4 days. The second group of patients (41 breast cancer patients with stage I, 9 patients with stage II) were followed by external beam radiotherapy on «Electra Synergy» after the BS during 3-5 weeks after the surgery. The single tumor dose was 2,5 gy. Time of EBRT ranged from 50 to 80 minutes. The post-operative drawbacks connected with radiotherapy are epidermitis- 88%, dermic ulcers – 0.1%. The average time of the treatment is approximately 35±4 days.

Conclusions: The analysis of the results showed that the using of IORT slightly increases the time of the operation, completely eliminates the possibility of skin manifestations of radiation therapy. Treatment regimen using IORT has several advantages and can be considered as an alternative treatment option in a strictly selected category of patients with LBC.

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# Conquer the tumor microenvironment: Phenotypic heterogeneity of human cancer using imaging mass cytometry

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Tumours are highly heterogeneous populations of cells, and measures of intratumoral heterogeneity (ITH) and diversity correlate with worse prognosis in many cancers. Emerging studies are highlighting functional interactions between subclones, as well as among subclones and components of the tumour microenvironment. A growing body of evidence indicates that the tumour microenvironment contributes to tumour growth and viability. However, these studies have focused on soluble factors without interrogating the spatial distribution of subclones defined by activated signalling pathways. In large part, this is due to limitations of currently available technology which does not allow for the detection of complex immunophenotypes in tissue sections. High parameter methods such as gene expression profiling or flow cytometry have been applied to study the tumour microenvironment (TME). However, data on cellular heterogeneity and rare cells is lost with gene expression studies, and the spatial relationship between the tumour and immune cells is lost with flow cytometry. We will circumvent these limitations by undertaking imaging mass cytometry (IMC), which allows for simultaneous measurement of 30-40 antigens while retaining the spatial organization of the sample. Our objective is to develop and optimize highly multiplexed assays for characterization of signalling heterogeneity in tissue microarrays of human tumours and describe the modelling cell signalling heterogeneity in cell line-based models to determine mechanisms of cell-cell interaction and communication in various tumours on the IMC platform. We have constructed an IMC panel of antibodies that combines markers for tissue architecture, tumour and immune cell phenotyping, and signalling pathway activation. Analysis of individual tumours demonstrates unique compositions of cell phenotypes between the edge and core of the tumour. Interestingly, while the tumour cells exhibit distinct phenotypes, the stromal cells are largely indistinguishable from one another. Methods developed here should be applicable for the study of the TME in different tumour types and could be used to identify additional biomarkers of response to immuno-oncology agents.

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# Combination therapies with epigenetic inhibitors for the treatment of soft tissue sarcomas

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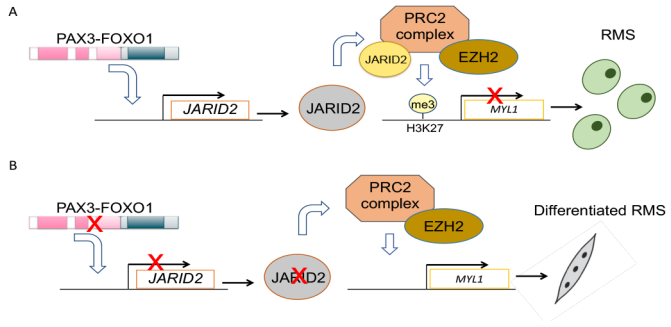
Differentiation therapy is an approach that has had notable success in a limited number of cancer types including acute promyelocytic leukaemia and neuroblastoma but remains underexplored for most tumour types. Therapeutic drugs have been shown to promote differentiation in preclinical models including soft tissue sarcomas (STS) that often resemble undifferentiated mesenchymal tissues. Rhabdomyosarcomas (RMS) are the most common paediatric STS and appear as developing skeletal muscle that are unable to terminally differentiate through aberrant recapitulation of developmental programs. Histone modifications are known to govern these developmental programs by controlling activities such as DNA transcription and cell differentiation. Enhancer of Zeste Homolog 2 (EZH2) confers histone methyltransferase activity to the Polycomb Repressive Complex 2 (PRC2), and is known to control stem cell renewal and differentiation.

We have shown that EZH2 and other members of the Polycomb Repressive Complex 2 (PRC2) play a role in the differentiation program of RMS and are required to maintain the undifferentiated phenotype of these tumours. Single agent modulation of EZH2 using a tool compound or clinical drug candidate results in modest differentiation of RMS cell lines, a phenotype that we show is augmented by combination with differentiating agents in vitro. Furthermore, we show that this combination can also be used to effectively reduce proliferation in synovial sarcoma lines in vitro. Thus combining inhibition of histone modifying enzymes with differentiating agents or other frontline therapies already in clinical use represent a novel potential avenue for therapeutic intervention for use in the treatment of STS.




*The Polycomb Repressive Complex 2 (PRC2) complex maintains the undifferentiated state of rhabdomyosarcoma (RMS) cells. (A) We have shown that the PAX3-FOXO1 fusion protein present in high-risk Alveolar RMS tumours directly regulates the expression of JARID2, a member of the PRC2 complex, which in turn methylates H3K27 on the promoter of myogenic genes to maintain the proliferative, undifferentiated state of RMS cells. (B) Silencing of JARID2, and other members of the PRC2 complex, results in removal of these methyl marks and ultimately to differentiation of RMS cells to a more benign state.*

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# Making 3D possible: Large scale organoid expansion using bioprocess design

**Mark Treherne**
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Organoids are three-dimensional 'mini-organs', which can be grown in culture and which recapitulate all the key features of the tissue from which they were derived. Organoids grown in 3D are widely accepted as being superior to traditional 2D cell culture systems, because they better represent the structure and function of their original tissue. This means they serve as better models and therefore have improved predictive ability in the drug discovery process. They can also be effectively deployed as a replacement for the use of animals in early preclinical studies.

A significant barrier to widespread adoption of organoids in drug discovery is that organoid production is a costly and highly labour-intensive process. Moreover, organoid culture is a skilled manual process, and thus there can be significant variability between operators.

Cellesce are currently developing bioprocessing systems for the efficient and standardised expansion of organoids in significant volumes, with the long-term goal of making organoid models more widely accessible to the drug discovery community. In doing so, organoid technology has significant potential to improve the predictive potential of efficacy and toxicity assays, and therefore rationalise the drug discovery process, reduce waste and replace the use of animal models.

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# Oral Cancer – Screwing and Early Diagnosis

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Head and Neck cancer is one of the most life-threatening malignancy and is ranked as the sixth most frequently occurring malignancies in human body. Oral cancer accounts for its fair share and almost all of the cancers are Oral Squamous Cell carcinomas. The oral cavity serves as the entry level for most of the carcinogens which makes it a potential target area for malignancies. The incidence rate of oral cancer is varied in its geographical pattern and is very high in South East Asia. The significance of oral cancer in recent years has increased because of its emergence in younger aged population. Inspite of its growing incidence the survival rate of Oral Cancer has not shown any significant progress. The foremost reason for less survival rate is contributed to the delay in its diagnosis and the predicament that is associated with definitive diagnostic modality. This points to the direction of the timing of diagnosis and the stage of the tumor. Oral cavity is functionally and anatomically complex in nature that its examination can fail even the well trained eye of an expert professional. Oral structures should be periodically examined and screened for any potential lesions. The anatomy of oropharynx is such that some areas are clearly visualised while few others pose difficulty for direct visualization. Premalignant lesions are missed or mistaken at this standpoint, while other lesions are misinterpreted due to the hindrance faced while palpating the posterior parts of oral tissues. Most of the patients initially ignore the symptoms relating it to a traumatic injury or a common oral sore, once the lesion starts its progression it invariably becomes asymptomatic and causes no evident discomfort. It is when the lesion enters the advanced stage, the symptoms become more evident and by the time it is in a more advanced state. Other important aspect which causes difficulty in definitive diagnosis is the selection of the biopsy site and sample tissue that is taken from the representative site. The tissue sample should have adequate quantitative pathological and normal cells for a prompt histopathological diagnosis. So, a specific paradigm should be designed for examination both visually and palpatory criterias. This paper brings to light the existing and adhered protocols in the diagnosis of Oral cancer. Additional informative inputs that would be valuable in the spot on diagnosis and futuristic screening techniques have been mentioned. Thus, an early diagnosis can cause less damage to oral structures during interventional treatment and give a better prognosis.

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# Epidemiology and clinical features of breast cancer in Rwanda

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**Background and Objectives**: Breast cancer is a growing crisis in the developing world. With a majority of breast cancer deaths occurring in the low income countries including Rwanda. The objective of this analytical study is to assess the epidemiology and clinical features of breast cancer in Rwanda.

**Methods**: Data were collected from August 2015 to January 2017 by considering information recorded from Out Patients Department (OPD), surgery and laboratory log books and from the archives of patients tested and diagnosed with breast cancer from three referral hospitals. Microsoft Excel and Statistical Packages for Social Sciences (SPSS 19.0) have been used for data entry and analysis.

**Results**: Brest cancer incidence rate frequency from August 2015 to January 2017 was 33.33% per semester. Amid the diagnosed breast cancer cases in that period, 97.04% of all cases arise in female whereas 2.87% arise in male. The most frequent breast cancer type was invasive ductal carcinoma with 80.43% and the least common were mucinous carcinoma and infiltrating medullary carcinoma with 1.08% for each. According to the age, both male and female between 51 and 60 years old are more likely to be affected with a frequency of 31.73%.

**Discussion and Conclusion**: Breast cancer frequency is increasing, because patients do not go for diagnosis and the few patients who go for it, are late and breast cancer is already advanced. Therefore we recommend to increase the awareness of breast cancer but also further researches to find affordable ways of breast cancer detection at early stages, for example we have started a research on rapid tests for breast cancer detection.

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# Difficulties in providing palliative care in rural India (West Bengal)- Experience of an NGO

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**Introduction**: As in any developing countries state of West Bengal in India has a huge burden of cancer patients in advanced stage coming from rural area where awareness regarding the usefulness of palliative care in rather poor.

**Objective**: Our goal is to give a pain free good quality of life in these advanced stage cancer patients. Objective of this study is to identify the main difficulties in achieving the above goal in a rural village setting in India.

**Method**: Advanced cancer patients in need of palliative care in various villages in of rural India were selected for this study. Their symptoms and managements in that rural surroundings were evaluated by an NGO (under the guidance of a senior palliative care specialist) working in that area. An attempt was made to identify the main obstacles in getting proper palliative care in a rural setting.

**Results**: Pain, fatigue are the main symptoms effecting these patients. In most patients pain and other symptoms control were grossly inadequate due to lack of properly trained manpower in the rural India. However regular homecare visits by a group of social workers were of immense help in the last few months of life. NGO team was well guided by a palliative care specialist.

**Conclusion**: There is a wide gap of trained manpower in this filled in rural areas of India. Dedicated groups from rural area itself need encouragement and proper training, so that difficult symptoms can be managed locally along with necessary social and psychological support to these patients.

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# Study of mTOR gene expression in plasma based microRNA-7 / Chitosan Complexes in Hepatocellular carcinoma cell lines

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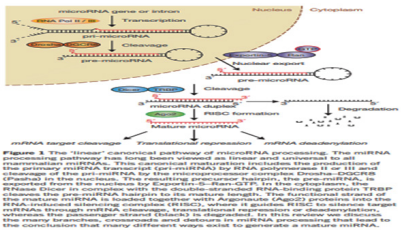


**Figure 1** The "linear" canonical pathway of microRNA processing. The miRNA processing pathway has long been viewed as linear and universal to all microRNAs (miRNAs). It begins with the transcription and 5′ capping of the primary miRNA transcript (pri-miRNA) by RNA polymerase II or III and cleavage of the pri-miRNA by the microprocessor complex Drosha–DGCR8 (Pasha in flies and worms) to release the pre-miRNA hairpin, which is exported from the nucleus by Exportin-5–Ran-GTP. In the cytoplasm, the RNase Dicer in complex with the double-stranded RNA-binding protein TRBP cleaves the pre-miRNA hairpin to its mature length. The functional strand of the mature miRNA is loaded together with Argonaute (Ago2) proteins into the RNA-induced silencing complex (RISC), where it guides the recognition of target mRNAs through mRNA cleavage, translational repression or deadenylation, whereas the passenger strand (black) is degraded. In this review we discuss the many branches, crossovers and detours in miRNA processing that lead to the conclusion that many different ways exist to generate a mature miRNA.

MikroRNAs are small, endogenous and non-coding RNA molecules which regulate gene expression. Recent studies show that deregulation of miRNAs have been associated with different diseases including cancer. Therefore, miRNAs are important therapeutic target in cancer. However, major obstacles of usage miRNAs in therapy are stability, rapid clearance and internalization. For this reason, it is important in terms of therapy with appropriate carrier system to the cells. Aim of this study is to investigate efficacy (invasion, apoptosis and cell proliferation) and usability in hepatocellular carcinoma (HCC) cancer cell lines (Hep3B and HepG2) of polyplexes forms of chitosan and miR-7 mimic. miR-7 mimic and chitosan complex was prepared. In vitro characterisation of these complex was done. With these dosage have used to investigate mTOR protein levels by using ELISA assays and invasion, apoptosis and cell proliferation assays have done. Our studies show that chitosan/miR-7 complex was internalized stably to cancer cells, thus deregulated miRNA levels repaired. Invasiveness of cancer cells was reduced. Chitosan complexes were shown to be safe and efficient delivery system for miRNA.

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# Dosimetric analysis in patients of breast cancer treated with image based high dose rate multicatheterinterstitial brachytherapy as a boost following whole breast irradiation

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**Background**: Breast conserving surgery followed by adjuvant radiotherapy has been established as the standard of care. The rationale for use of boost following whole breast irradiation is to decrease the risk of local relapse in the tumor bed area.

**Purpose**: To analyse the dosimetric data and perform quality assessment of treatment plans in patients of breast cancer treated with image based high dose rate interstitial brachytherapy as a boost following whole breast irradiation.

**Materials and methods**:Fifteen patients who received boost with interstitial implant were included. All patients underwent breast conserving surgery and received whole breast irradiation with dose of 40Gy in 16 fractions to breast and drainage area. Under ultrasound guidance, cavity was identified and needles were inserted into and surrounding the lumpectomy cavity to deliver adequate dose to tumor bed. The target volume was contoured on CT images. The total dose delivered by brachytherapy boost was 15 Gy in 5 fractions at 3 Gy per fraction with an inter-fraction interval of 6-8 hours. Dosimetric indices were calculated to assess the quality of interstitial implant.

**Results**:The mean age of patients was 43 years. The mean tumor size was 2.6 cm with range of 1.5-4.2 cm. The mean treated length was 4.7 cm (range 3.5-7 cm). The median number of needles inserted were 8. The mean D90 of target volume was 103±15%. The mean V100 for target volume was 53.1 cc (range 24-81.6cc).The mean coverage index,dose homogeneity index, over-dose volume index, dose non-uniformity ratio, conformal index, uniformity index and quality index were 0.87±0.07, 0.78 ± 0.04, 0.43±0.06, 0.42±0.07,0.87±0.07, 1.06±0.06 and 1.12±0.07, respectively.

Conclusion:Analysis of dosimetric parameters is important to evaluate the quality of implant as it corelates with the long-term outcome as well as acute and late effects. These dosimetric indices help in estimating the risk of developing local relapse and breast fibrosis.

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