COMMENTED POSTER
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INVESTMENT OF THE UNIFIED HEALTH SYSTEM IN SCREENING MAMMOGRAPHY IN BRAZIL, 2008–2017

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Objective: To evaluate the investment of financial resources applied by the Unified Health System (SUS), in the mammographic screening performed by in Brazil, from 2008 to 2017. **Methods:** A prospective study where the number of mammograms performed by the SUS was observed in women aged 50–69 years and the value approved for payment of the respective examinations, available in the Outpatient Information System (SIA/DATASUS). The amount approved for payment was compared with the amount established for the SUS (R$ 45.00) and the number of exams performed. **Results:** In the period evaluated, R$ 968,567,514.42 were invested in mammographic screening by the Union, for a total of 22,214,981 examinations performed, at a unit value of R$ 43.60. When comparing this value with that established by the SUS (R$45.00), it is possible to infer a surplus for the System of R$31,106,630.58, which would represent the accomplishment of approximately 691 thousand new exams. On the other hand, the amount paid per examination remained fixed in the 10 years evaluated in the study. In a simple analysis of monetary restatement in relation to inflation in the period evaluated, when applying the Extended Consumer Price Index (IPCA), the expected value for payment of the exam in 2017 would be approximately R$ 79.41. **Conclusion:** The scenario evaluated suggests that there were resources for the mammographic screening, but not enough to increase the coverage of the exams and maintain the established value for the SUS, of R$ 45.00.

RETURN TO WORK ITS IMPACT ON THE QUALITY OF LIFE OF BRAZILIAN BREAST CANCER PATIENTS

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Objective: To evaluate the impact of return to work on the quality of life of breast cancer patients, and factors related to non- return to work. **Method:** A prospective, cross-sectional study approved by the Research Ethics Committee (1180/2016). The study was performed in patients who worked in the during 2012–2014; clinical stage 0 to III, age 25–60 years old. Based on a previous National study, a sample of 304 women was estimated. Standardized clinical records evaluated all patients, and the questionnaire EORTC QLQ-C30, EORTC BR-23, SPADI and HADS were also applied. Patients were randomized to a 1:1 to perform physical therapy examination, which was based on shoulder goniometry, hand dynamometry, and limb volume. Data were analyzed by the chi-square test and the Mann-Whitney test. Univariate and multivariate analysis were performed. **Results:** 304 were included, where 163 were submitted to physiotherapy evaluation. The mean age and schooling was 46.1 years and 11 years, respectively. 49.3% underwent conservative surgery; 51.5% axillary lymphadenectomy; 86.1% received chemotherapy, 84.2% had adjuvant hormone therapy, and 87.7% had radiotherapy, but 46.2% had radiotherapy on the supraclavicular fossa. At the moment of the diagnosis 50.7% exerted manual activities, 28.0% intellectual activities; and 21.4% manual and intellectual activities. 94.7% stopped working during treatment. 84.9% received social security benefits. 54.0% returned to work after treatment. The women who returned to work presented lower age ($p<0.001$), higher schooling ($p<0.0001$), higher income ($p<0.001$), and smaller initial tumor size ($p=0.008$). These patients were generally submitted to sentinel lymph node ($p=0.02$), received adjuvant chemotherapy ($p=0.004$), and had intellectual demand work ($p<0.001$). There was an overall significant decrease in work capacity. Patients whose had loss of strength in the hand had a 2.2-fold risk of non-return to work ($p=0.02$). In the multivariate model to evaluate the not return to work, pre-treatment variables were age, schooling and clinical staging. Before treatment, lymphadenectomy increased 1.9 times the risk of not returning to work, and self-reported loss of strength in the hand 2.9 times. Physical demand work has raised the risk by 2.7 times. The women who returned to work presented a better quality of life through the EORTC QLQ C30 questionnaire; by BR23 presented higher scores related to body image and sexual function; by SPADI lower scores in relation to disability and pain; and by HADS lower scores related to anxiety and depression. **Conclusion:** 54% of patients did not return to work after breast cancer treatment. It was influenced by age, schooling, previous type of activity, axillary treatment, and physical sequel related to loss of strength on the hand. Return to work improved patients' quality of life.

AGE OF DIAGNOSIS AND BODY MASS INDEX IN BREAST CANCER PATIENTS: ANALYSIS OF A BRAZILIAN REFERENCE CENTRE

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Objetives: Breast cancer affects about 59,000 Brazilian women annually according to data from INCA 2018 (National Cancer Institute) and 14,388 deaths are related to the disease. There are few data about the age specific incidence in our Country and almost anything about the prevalence of obesity in our population. Pérola Byington Hospital is one of the most important cancer centers specialized breast cancer treatment in Brazil and we are responsible for treating about a thousand new cases of breast cancer annually. **Methodology:** We have created a web-based system that helped us to input information about the breast cancer cases treated in our hospital. This study was performed at the Pérola Byington Hospital evaluating the age of diagnosis and their body mass index (BMI) before the treatment. Descriptive data is shown. **Results:** There were 8,420 cases of breast cancer enrolled in our analysis and most of our cases were diagnosed with 50 or more years old (n=5.507) which corresponds to 65.41%. The patients' age ranged from 18 to 93 years, with a median of 54 years. Only 1.23% of the cases were diagnosed below 29 years of age and 33.2% of the cases were between 30 and 49 years. There was a considerably number of cases that have been diagnosed between 40 and 49 years old (n= 2.044) which correspond to 24.28% of our population. We made an analysis to see if from 2011 to 2017 there was any difference in incidence specified by age and it was not statistic significant. Regarding the BMI we were able to recover 5,878 cases of breast cancer and the majority of our patients were obese or overweigh by the time of diagnosis (65.8%). **Conclusions:** In our analysis we have found that there are a lot of breast cancer in young patients and we have to take that in account to treat better our patients, there is no increase during the last years of young patients in our data. Most of our patients are obese or overweight at the time of diagnosis of breast cancer.

MICRORNAS AS BIOMARKERS FOR BREAST CANCER PROGNOSIS: A SYSTEMATIC REVIEW

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Objectives: Breast cancer is an important health problem worldwide and the identification of prognostic markers in breast cancer is important in order to establish the most successful treatment for each patient. MiRNAs are non-coding RNAs, which modulate the expression of more than 50% of human genes at the post-transcriptional level. Deregulation of miRs is described in many types of tumors leading to their acting as tumor suppressors or oncogenes. This systematic review of the literature aimed to highlight tumor miRNA quantification, by real time PCR, as prognostic biomarkers in breast cancer. **Methods:** We systematically searched the PubMed database, in order to identify eligible studies and 1457 articles were initially selected. After reading the abstracts, 74 articles were read in complete and 20 studies were included in the review. **Results:** Twenty studies investigating the association between tumoral miRNA expression levels (predictive factors) and the prognostic in breast cancer patients were included in the review. MiRNA-21 and miRNA-200b were the most commonly investigated miRNA in breast cancer prognosis. Lymph node metastasis was significantly associated with the overexpression of miRNA-21, miRNA-301 and miRNA-370, and also to the under expression of miRNA-124, miRNA-127, miRNA-129-5p, miRNA199-5p, miRNA-206, miRNA-218, and miRNA-339-5. Distant metastasis was associated to miRNA-204 under expression. Tumor size was associated with the overexpression of miRNA-21 and miRNA-301, and also to under expression of miRNA-29b and miRNA129-5p. In relation to prognosis, lower survival rates were associated with the overexpression of miRNA-21, miRNA-301 and microRNA- 711, and with under expression of miRNA-15a, miRNA-29b, miRNA-124, miRNA-129-5p, miRNA-199b-5p, miRNA-200b, miRNA-204, miRNA-206 and miRNA-218. Higher survival rates were associated with the overexpression of miRNA-339-5 and miRNA-127 On the other hand, higher survival rates were associated with overexpression of miRNA-339-5 and miRNA-127, and also to under expression of miRNA-210. **Conclusion**: According to the results, preclinical and clinical investigation performed on tissue-specific miRNAs can be considered as novel promising biomarkers for prediction of prognosis in breast cancer patients.

EFFECTS OF [10]-GINGEROL IN COMBINATION WITH DOXORUBICIN ON TRIPLE NEGATIVE BREAST CANCER *IN VITRO* AND *IN VIVO*

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Objective: Triple negative breast cancer (TNBC) often metastasizes to bones, lungs and brain. It does not respond to current target therapies, and thus, limited treatments are available, especially for late stage disease. We have previously shown that [10]- gingerol has cytotoxic and anti-metastatic properties against TNBC *in vivo* and *in vitro*. To further mimic a clinically relevant scenario, which often involves the use of multiple drugs, we evaluated the effects of [10]-gingerol in combination with doxorubicin for TNBC treatment. **Methods**: TNBC cells (MDA-MB-231 and 4T1Br4) were treated with [10]-gingerol (10G), doxorubicin (DOX) or both (10G+DOX) and assayed for viability, colony formation and apoptosis. Next, TNBC cells were inoculated orthotopically into the mammary fat pad of female mice. When tumours became palpable, mice were treated with saline solution (Control), 10G (5-10mg/kg daily), DOX (3mg/kg twice a week) or a combination of both (10G xmg+DOX xmg). Body weight and primary tumour growth were monitored throughout the entire experiment (30 days). Upon euthanasia, blood was collected to analyse the presence of circulating tumour cells (CTCs), as well as toxicity markers. Lungs, bones and brain were harvested for metastatic burden assessment. **Results**: The association of 10G and DOX had additive inhibitory effects on viability and colony formation and increased apoptosis in TNBC cells. Regarding to the *in vivo* experiments, 10G, especially when combined with DOX, dramatically reduced primary tumour growth, as well as the incidence and/or the number of viable circulating tumour cells. As a result, metastasis was also impaired. Moreover, the combination (10G+DOX) not only had the aforementioned additive antitumour and antimetastatic effects, but also attenuated doxorubicin-induced toxicity. Remarkably, only 7/15 mice treated with DOX remained alive at end-point, and this number increased to 11-12/15 when mice received 10G alongside (5 or 10 mg/kg, ip, daily, respectively). We also noticed attenuation in weight loss and hepatotoxicity (AST and ALT levels in serum) when the combination regimen was used. Additional analysis to elucidate the molecular mechanisms involved in these effects are ongoing. **Conclusion**: Taken together, our data indicate that [10]-gingerol could be used as adjuvant/complementary therapy for TNBC, enhancing the anticancer activity and attenuating undesired side effects of conventional chemotherapeutic agents.

ANALYSIS OF POLYMORPHISMS IN THE TP53 GENE IN PATIENTS WITH CLINICAL DIAGNOSIS FOR HEREDITARY BREAST CANCER

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Breast cancer is the second most frequent type of cancer in the world and the most common among women. Of the total number of cancer diagnosis each year, it is estimated that 5% to 10% are hereditary, usually caused by mutations in tumor suppressor genes. Mutations or polymorphisms in the TP53 gene are the most common genetic alterations in human malignant tumors. More than 85 polymorphisms in the TP53 gene have been identified, with PIN2 located in exon 2, PIN3 located in exon 3 (16pb doubling) and PEX4 located in exon 4 (Arg72Pro). Studies have reported that PIN2 has no pathogenic significance, however PEX4 and PIN3 have inconclusive results, and there may be some association between the risk of developing cancer and the presence of these variants. The objective of this work was identify the polymorphisms present in exons 2 to 4 of the TP53 gene in patients with clinical diagnosis for hereditary breast cancer. For the study, 5 mL of blood were collected from 55 female patients treated at the Hospital das Clínicas of the Federal University of Goiás. After collection, the samples were submitted to DNA extraction, Polymerase Chain Reaction (PCR) and sequencing Sanger of exons 2, 3 and 4 of the TP53 gene. The results showed that three polymorphisms were found: 31 (56.3%) had the PIN2 polymorphism, 20 (36.3%) had PEX4, and only one (1.8%) presented PIN3, some sequences presented more than one polymorphism, only 16 (29.0%) did not present any polymorphism in the analyzed regions. In addition to these three polymorphisms, an unknown polymorphism was verified in exon 3, which is not present in the databases nor in the literature, suggesting that it may be a polymorphism not yet described until now. Patients' charts were also analyzed and no association between polymorphisms and age at diagnosis, treatment response, and patient survival were identified. These results contribute to the identification of polymorphisms present in the TP53 gene and show the relatively high frequency among breast cancer patients. However, further studies are needed to better understand the influence of these polymorphisms on the TP53 gene and the risk of developing hereditary breast cancer.

COMPARISSON BETWEEN MORPHOLOGICAL ASPECTS ON THE MAMMARY ULTRASSONOGRAPHY OF BREAST MALIGNANT NEOPLASIES AND THE IMMUNOHISTOCHEMISTRY PROFILE OF THESE TUMORS

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Objective: Compare the morphological aspects on the mammary echography of malignant tumors with the immunohistochemistry profile of these tumors and identify morphological parameters that are related in a significant manner with immunohistochemistry variants. **Methods**: We compared the ultrasonography morphological features defined according to the ACR BI-RADS – US® on its first edition (shape, posterior acoustic features, margins, lesion boundaries, echo pattern and orientation) with the immunohistochemistry profile, defined by hormone receptors (i.e. estrogen receptors (ER) and progesterone receptors (PR)), human epidermal growth factor 2–neu receptor (HER2) and Ki67 antigen of 518 malignant breast tumors. Statistically significant associations were defined as $p \leq 0.05$ on the Pearson's chi-square tests and Monte Carlo procedure. **Results**: We found a negative relation between hormone receptors (ER and PR) and the characteristics enhancement and absence of posterior acoustic features, abrupt interface and microlobulated margin. Also, we found a negative relation between ER and oval shape and parallel orientation, as well as negative relation between PR and round shape and complex echo pattern. Our results also comprehend positive association for ER and PR with the characteristics shadowing, irregular shape, echogenic halo and spiculated margins. There was also positive association between non-parallel orientation and ER. We found positive association between expression of Ki67 antigen and microlobulated margins. It was possible to demonstrate a relation among basal like tumors and posterior acoustic features (enhancement or no posterior acoustic feature), oval or round shape, abrupt interface, microlobulated margin and parallel orientation. Tumors that present shadowing or lesion boundary with echogenic halo at the ultrasonography were less likely to be identified as basal like. **Conclusion**: we found certain statistically significant associations between the immunohistochemistry profile of the tumors and the ultrasonography features.

TNM8 BREAST CANCER CALCULATOR: A TOOL FOR BREAST CANCER STAGING ACCORDING TO THE TNM 8TH EDITION

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Objectives: To develop an APP to help healthcare professionals around the world in the breast cancer staging process according to the new AJCC criteria. **Methodology:** Extensive revision of the AJCC Cancer Staging Manual 8th Edition and the Updated Breast Chapter with a high improvement of the knowledge in this field. Creation of the medical interface for computer interface. **Results:** Development of the software named TNM8 Breast Cancer Calculator that is an updated, complete, intuitive, and user-friendly tool for Breast Cancer Staging. All data and definitions are based on the Updated Breast Chapter - AJCC Cancer Staging Manual 8th Edition, released on November 10th, 2017 that included the classic Anatomic Stage Group and the new and revolutionary Prognostic Stage Group (divided in Clinical Prognostic Stage and Pathological Prognostic Stage) with the incorporation of biomarker factors. The prognostic factors included are: Tumor Grade (G), HER2, Estrogen Receptor (ER) and Progesterone Receptor (PR). Genomic Profiles were also incorporated as a prognostic factor for eligible cases (pT1-T2 N0 M0 HER2- and ER+) in the Pathological Prognostic Stage. This App provides the quantification of the category change of the Clinical Prognosis Stage (cPS) and also the Pathological Prognostic Stage (pPS) in relation to the Anatomic Stage (AS) expressed in the Staging Line with the symbol +1, +2, +3 in case of worsening in the Prognostic Staging or -1, -2, -3 in case of improvement in the Prognostic Staging. When no symbol is shown, it is because the AS and cPS or AS and pPS are identical. This App has other function that shows Oncotype DX® / Genomic Profile field only in some setting when the genomic test is potentially indicated (pT1-T2 N0, HER2- and ER+). The TNM8 Breast Cancer Calculator got the approval of the AJCC and American College of Surgeons. **Conclusion:** The new TNM for breast cancer changed the process of breast cancer staging. These updates will provide additional precision and flexibility to the staging system but with a complex process. For a correct staging process, doctors need to use complex tables or can use the smart tools to help them in this process. TNM8 Breast Cancer Calculator is very useful for breast surgeons, surgical oncologists, medical oncologists, radiation oncologists, pathologists, radiologists, medical students, scientists, researchers, and all healthcare professionals working in the field of breast oncology.

PROSPECTIVE STUDY OF POSTOPERATIVE WHOLE BREAST RADIOTHERAPY FOR PATIENTS WITH LARGE AND PENDULOUS BREAST: A CLINICAL AND DOSIMETRIC COMPARISONS BETWEEN SUPINE AND PRONE POSITIONS

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Introduction: Adjuvant radiotherapy is the standard treatment following breast conserving surgery (BCS). Irradiation after BCS in women with large and/or pendulous breasts is a challenge for radiation oncologists. Increased radiation related toxicity and worse cosmetic outcome was found in these patients. Prone breast irradiation aims to improve some of the technical limitations associated with treating large and pendulous breasts and it may limit radiation doses to organs at risk (OAR) such as lung and heart. **Objectives:** The goal of this study is to compare dosimetric parameters in prone versus supine position in a cohort of women with pendulous breasts receiving Radiotherapy after conservative surgery and the severity of cutaneous toxicity in these patients. **Methods:** Early-stage breast cancer patients with large or pendulous breasts undergoing BCS participated in this study. CT-based treatment plans were made in each position, and various dosimetric parameters for the breast and OAR were calculated to compare the supine and prone radiotherapy plans. The actual treatment was delivered in the position regarded as better. The patients were followed during the treatment to evaluate the skin and the grade of radiodermatitis were registered. **Results:** From 2016 to 2017, 26 patients were prospectively accrued. The median lung dose and the V20 (lung volume that receives 20 Gy) were significantly lower in the prone position ($p<0.0010$). The homogeneity index and the contralateral breast dose were significantly lower in the supine position ($p=0,006$ and $p< 0,01$ respectively). The other variables (V25 and heart median dose) showed no significant differences between two positions. By comparing two plans, the prone position was chosen in 73% of the patients. In the prone position, grade 2 dermatitis were seen in 26%, whereas 42.8% of patients treated in the supine position had grade 2 and no cases of grade 3 dermatitis, although without a statistical significance ($p=0.33$). **Conclusions:** Prone breast irradiation lowers lung dose significantly when compared to supine position. Although without a statistical significance, there was a trend towards a reduction in skin dermtititis when patients were treated in prone position.

HAND2 AND ER EXPRESSION IN BREAST CANCER

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Objectives: To verify the immunohistochemical expression of Heart and Neural Crest Derivatives Expressed Transcript 2 (HAND2), a tumor suppressor protein, .in breast tissues with and without breast cancer. To correlate the expression of HAND2 with estrogen receptor (ER). **Methods:** In this case-control study, 19 formalin–fixed, paraffin-embedded tissues were obtained for pathological archives analysis. Tissue sections of breast tissue derived from benign conditions (n=10) and breast cancer (n=9) were analyzed for the intensity of the staining with 3,3'-diaminobenzidine using rabbit polyclonal antibody against HAND2 (Ab60037), at dilution 1:50 at pH 9; ER was analyzed using clone 1D5, monoclonal, Dako) diluído a 1/100. ImageJ software with "color deconvolution" was used for analysis of the expression of these proteins. Statistical analysis was performed using unpaired t-test and correlation of Pearson . The sample size was calculated in order to have a power of 95%, an alpha error of 1% to identify an increase in the primary outcome measure from 15 in the control group to 44 in the experimental group. **Results:** HAND2 expression (mean±SD) in the breast tissue was 15.5±1.9 (cancer) versus 44.9±7 (breast cancer) (p=0.0006). Its expression was present in the nuclear and cytoplasmic compartments of the cells. No correlation was observed between ER and HAND2 (Pearson r = -0.28 (95%CI -0.6–0.22; p=0.2). **Conclusions:** The immunoexpression of HAND2 is reduced in breast cancer, compared with normal breast tissue. The expression of HAND2 is not correlated to ER expression These findings may guarantee further research as a potential independent prognostic biomarker.

EFFECTIVENESS OF DIFFERENT ACCELERATED PARTIAL BREAST IRRADIATION TECHNIQUES FOR THE TREATMENT OF BREAST CANCER PATIENTS: SYSTEMATIC REVIEW USING INDIRECT COMPARISONS OF RANDOMIZED CLINICAL TRIALS *[EFFECTIVENESS OF DIFFERENT APBI TECHNIQUES]*

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Background: Numerous accelerated partial breast irradiation APBI techniques are available for clinical practice. This systematic review was conducted to compare the effectiveness of different APBI techniques for the treatment of breast cancer patients. **Methods:** Systematic review of randomized controlled trials of APBI versus WBI. The data from APBI studies were extracted for the analyses. Indirect comparisons were used to compare different APBI techniques. **Results:** Ten studies fulfilled the inclusion criteria. A total of 4343 patients were included, most of them with tumor stage T1-T2 and N0. Regarding APBI techniques, six trials used external beam radiation therapy; one intraoperative electrons; one intraoperative low-energy photons; one brachytherapy; and one external beam radiation therapy or brachytherapy. The indirect comparisons related to 5-years local control and 5-years overall survival were not significantly different between APBI techniques. **Conclusions:** Based on indirect comparisons, no differences in clinical outcomes were observed among diverse APBI techniques in published clinical trials that formally compared WBI to APBI. However wide confidence intervals and high risk of inconsistency precluded a sound conclusion. Further head-to- head clinical trials comparing different APBI techniques are required to confirm our findings. Studies comparing different techniques using individual participant data and/or real-life data from population-based studies/registries could also provide more robust results.

THE ROLE OF PALLIATIVE RADIOTHERAPY IN LOCALLY ADVANCED BREAST CANCER REFRACTORY TO NEOADJUVANT CHEMOTHERAPY AND UNRESECTABLE

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Objectives: Locally advanced breast cancer (LABC) is a major health problem in developing countries, including Brazil. The standard treatment for LABC is neoadjuvant chemotherapy, with or without anti-Her2 therapy, followed by surgery, radiotherapy (RT), and adjuvant systemic treatment if appropriate. However, there are few data in the literature addressing alternatives when neoadjuvant chemotherapy fails to reduce the tumor for surgery. Nearly one third of LABC are resistant to multimodal neoadjuvant treatment remaining unresectable. As an alternative to downsize tumor and allow surgical removal, palliative radiotherapy has been reported as an option. The aim of this study is to verify the role of palliative radiotherapy in the treatment of LABC, once considered unresectable and not responding to neoadjuvant chemotherapy. **Methods:** It is a retrospective study including 25 patients who had non-metastatic LABC treated with neoadjuvant chemotherapy and who were not eligible for surgical resection; these patients were submitted to salvage radiotherapy between January 2017 and January 2018 at Araujo Jorge Hospital and Cebrom clinic. All patients were followed by photography analysis and by a single observator. **Results:** During one year, 25 patients were included, with a median age of 55 (30–80) years and the average was 52 years old. The most frequent clinical stages were IIIA and IIIB, corresponding to 18.8% and 81.2%, respectively, characterized by bleeding and secretion, mostly with pain; mean tumor size was 14 (3–25) cm, and 22 patients (88.4%) had nodal involvement. Neoadjuvant chemotherapeutic regimens were prescribed to 88% of the patients. Radiation dose initially prescribed was 70 Gy divided into 35 fractions, however the average dose received was 50,2Gy; At the end of radiation therapy, the median tumoral response was 55% (10–100%) and the average was 51%. After 104 days post RT the average tumor response was 86%. After 70 days and 120 days post radiotherapy, 2 patients (8%) had their tumors downsized and underwent mastectomy, respectively. The overall survival will be still analysed. **Conclusion:** Neoadjuvant radiotherapy is an effective treatment to downsize breast cancer tumors with low or absent response to chemotherapy, as well as coping with local control. In this study, the radiation treatment was responsible for 86% of tumor downsize, with great improvement of the bleeding and tumor secretion.

THE IMPACT OF RADIODERMATITIS IN QUALITY OF LIFE OF PATIENTS WITH BREAST CANCER DURING TREATMENT: A PROSPECTIVE LONGITUDINAL STUDY

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Objective: To investigate the influence of radiodermatitis severity on the quality of life (QOL) of women with breast cancer (BC) throughout radiotherapy (RT). **Methodology:** A prospective longitudinal study conducted with 100 BC patients evaluated weekly during RT and three months after treatment. The questionnaire The Dermatology Life Quality Index (DLQI) and Radiation Therapy Oncology Group (RTOG) Scale were used to evaluate QOL and radiodermatitis, respectively. The Generalized Estimated Equations (GEE) were used to examine the association between the total score of QOL and their domains (symptoms and feelings, daily activities, leisure, personal relationships, work/school and treatment), time of RT and the radiodermatitis score, controlled by confounding factors (age, years of study and economic classification). Estimated marginal means and 95% confidence intervals were compared pairwise by applying Sequential Sidak for multiple tests. **Results:** The total QOL score, as well their domains (work/school, leisure, daily activities, symptoms and feelings) were significantly associated with the time of RT ($p \leq 0.001$), with the radiodermatitis score ($p \leq 0.001$) and with the interaction time of treatment and radiodermatitis score ($p \leq 0.001$). When assessing the post-hoc (sidak sequencial), it was identified that the worst QOL scores were in the presence of grade 3 (mean = 6.00) in T3 and grade 4 (6.50; 7.00) in T5 and T6, respectively, and this difference was statistically significant. Considering the domain signs and symptoms, we recognized a worse score in the presence of grade 4 (3.00) in T6. Regarding to the work and school domains and daily activities, the worst scores were identified in T5, in patients with grade 0 (4.00) and grade 3 (2.50), respectively. The leisure domain had a worse score in T3 in grade 3 (3.00). **Conclusion:** Women with BC had a negative impact on QOL during RT, with the greatest impact related to severe radiodermatitis. Actions aimed at minimizing the impairment in QOL need to be adopted to transform this exhausted process, less traumatic and easier to finalize.

A PROTECTIVE EFFECT OF MORNING RADIOTHERAPY ON SKIN TOXICITY IN PATIENTS WITH BREAST CANCER

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Objective: To evaluate the predictive factors of radiodermatitis, including the time of day in which the patients were treated. **Methodology:** A prospective cohort study conducted with 100 breast cancer (BC) patients evaluated weekly during radiotherapy (RT) and three months after treatment. Survival analysis considering as the end point the occurrence of radiodermatitis grade ≥2, according to Radiation Therapy Oncology Group (RTOG) was conducted by univariate and multivariate Cox regression. **Results:** In the multivariate analysis, RT in the afternoon (0-3 pm) (HR= 1.566, p=0.042), was significantly associated with the early occurrence of radiodermatitis, when compared with the morning (7-10 am), indicating a potential effect of chronotherapy regarding this adverse event. In the univariate and multivariate analysis, moderate brown skin phototype (HR=1.586, p=0.042; HR=1.706, p=0.022, respectively) and dark or black (HR=4.517, p≤0.001; HR = 5.336, p≤0.001, respectively) when compared with white or light white was significantly associated with the early occurrence of radiodermatitis. The tangential field separation >21 cm (HR=2.550, p=0.009, HR=2.923, p=0.003), that in women submitted conservative surgery indicates indirectly large breast size, when compared tangencial field separation <18 cm was also significantly associated with the early occurrence of radiodermatitis. **Conclusion:** Women with BC, especially when submitted to conventional techniques, common in low-income countries and under development and those with the presence of these risk factors (Dark Brown or black phototypes and tangential field separation >21 cm in women submitted conservative surgery) should be submitted to RT in the morning. It is also suggested the development of researches that test products that can act directly on the pathway of production of melanin, aiming to prevent this adverse event.

EXPRESSION OF PRO- AND ANTIANGIOGENIC VEGF-A ISOFORMS AND SPLICING REGULATORY FACTORS IN BREAST CANCER

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Objectives: The aim of this work was to analyze the expression of pro- and antiangiogenic *Vascular Endothelial Growth Factor* (*VEGF-A*) gene isoforms generated by alternative splicing in samples of breast cancer and non-tumor adjacent tissues, and to investigate the involvement of genes encoding the regulatory proteins SRPK1, SFRS1, SRSF5, and SRSF6 in the *VEGF-A* gene alternative splicing. **Methods:** The expression of *VEGF-A*$_{165}$, *VEGF-A*$_{165}$*b* isoforms and genes encoding the splicing regulatory proteins of 50 breast cancer samples and 43 adjacent non-tumor tissues were analyzed by real-time quantitative PCR. The values of relative quantification (RQ) in tumors were analyzed by Wilcoxon Signed Rank Test. Spearman correlation was used to evaluate the correlation between the expression of the genes encoding regulatory proteins and the *VEGF-A* isoforms. Binary Logistic regression was used to analyze the association between the expression of *VEGF-A* isoforms and metastasis. P≤0.05 were considered significant. **Results:** The overexpression of *VEGF-A*$_{165}$ (median RQ=7.7, p<0.0001) and *VEGF-A*$_{165}$*b* (RQ=2.9, p<0.0001) isoforms was observed in breast tumors compared to adjacent non-tumor tissues. The expression of *SRPK1, SFRS1*, *SRSF5*, and *SRSF6* genes was significantly increased in breast tumors compared to non-tumor tissues (p<0.0001). The expression of *SFRS1*, *SRSF6*, *SRSF5* and *SRPK1* were positively correlated with both isoforms of *VEGF-A*. Down-expression of antiangiogenic isoform *VEGF-A*$_{165}$*b* was significantly associated with metastasis (OD=4.93; 95%CI 1.03–23.63; p=0.03). **Conclusion:** The overexpression of both pro- and antiangiogenic *VEGF-A* isoforms in breast cancer can influence in the treatment of this tumor type, because the currently used anti-VEGF-A therapies target both isoforms, which could prevent the antiangiogenic activity of VEGF-A$_{165}$b. The splicing regulatory factors SRSF1, SRSF6, SRSF5, and SRPK1 can contribute to alternative splicing of the *VEGF-A* gene. The expression of antiangiogenic isoform *VEGF-A*$_{165}$*b* is a relevant factor for the prognosis of patients with breast cancer.