Material and Methods: About 225 patients (mean age 45±6 years) presenting with variable morphology, histological grades and clinical stage of the breast carcinomas during January 2006 to January 2008 were included. The patients were assessed both clinically as well as expression of ER, PR and NE markers was determined by indirect immunohistochemistry. Positive staining was asserted following the criterion proposed in previous literature. The patients were followed up clinically from the departmental record for 3 years till January 2011.

Results: The findings of our study revealed that immunohistochemical staining of the histological tissue sections of 10.2%, 7.4% and 15.1% breast carcinomas demonstrated focal areas with mild to strong cytoplasmic staining of the tumour cells by CgA, NSE and HDC respectively. Individual subtypes when assessed revealed that most of the ductal carcinomas stained positively and strongly than other varieties. Our findings also depicted that HDC expression in detecting the NE foci in breast carcinomas was stronger and more sensitive than CgA and NSE ($P = 0.0063$) and that too even in PD tumours of which 8.2% were strongly positive as compared to CgA (2.0) and NSE (1.3%) ($P < 0.001$). No significant association was found between the NED of breast carcinomas and clinico-pathological or hormonal receptor status of the patients. As per the follow-up record of 3 years, either univariately nor taking account of various known prognostic factors, does focal NED appear to carry a special prognostic significance as disease recurrence occurred locally in 01 patient and distant metastases was found in none.

Conclusion: Out results suggest that NED, though present in breast carcinomas, particularly of ductal type, may characterize a subgroup of these tumours with no significant impact on patient prognosis. However, more perspective analyses with prolonged follow up should be carried out in our female patients to assess these NE differentiated carcinomas in terms of their prognostic implication and therapeutic choices.

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Impact in the Management of Patients After Pathology Second Opinion in Breast Cancer

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Background: A second opinion in pathology may be requested by clinicians, when a patient is referred from another hospital for diagnosis and treatment. In patients with breast cancer, the pathology report contains valuable information about the diagnosis, but also related to prognosis and therapeutic response. We report the experience with second opinion in breast pathology, in selected patients consulting the Breast Oncology Unit at our institution.

Materials and Methods: Two hundred and four cases referred to the Breast Oncology Unit were selected for second opinion after clinical evaluation, between 2002 and 2011. The cases reviewed included 92 core needle biopsies, 98 surgical biopsies, and 14 fine needle aspiration cytologies. A case was classified as major change in second opinion when the findings had the potential for significant change in treatment or prognosis. A case was considered to represent minor change, when these did not alter significantly the treatment or prognosis.

Results: Concordant results were found in 162 (79.4%) diagnoses. In 42 cases (20.5%) the pathology review showed changes. Twenty-eight (13.2%) patients were classified as major changes. In 4 of this 28 patients, breast cancer metastasis diagnosed in an axillary node turned to be non mammary breast cancer (one was a melanoma, two were lung metastasis and one was a cutaneous anexal tumor). Another patient with a diagnosis of breast cancer metastasis in a brain biopsy was changed to lung metastasis to the brain and the last one diagnosed as breast cancer was changed to lung metastasis in the breast. Two patients diagnosed with breast cancer changed to benign breast lesions. In 4 patients there was a change in estrogen receptor status, three from negative to positive, and one in the opposite way. The Her2-neu status changed from positive to negative in five cases. Five patients with a diagnosis of infiltrating ductal carcinoma (IDC) turned to be carcinoma in situ (DCIS) in three, and microinvasive in two. Four patients classified as CDIS changed to IDC, and two cases changed from microinvasive carcinoma to DCIS. Fourteen patients (6.8%) had minor changes after the pathology second opinion. Most of them included changes in atypical hyperplasia to typical. Others reviews resulted in changes in progesterone receptor status that did not change treatments.

Conclusions: Second opinion in breast pathology may uncover significant discrepancies that impact in patient management and prognosis. Major discrepancies are most frequently related to the assessment of the degree of invasion of breast carcinoma and the result of immunohistochemical studies. However, the assessment of axillary lesions and distant metastasis in patients suspected of having breast cancer that may reveal non-mammary tumors, together with the diagnosis of benign proliferative lesions that simulate malignancy, may also severely affect the patient's treatment and prognosis.

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Ductal Carcinoma in Situ of the Breast − Modified Black Nuclear Grading System Revisited

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Background: This study aims to determine the pathologists agreement of modified Black nuclear grading system and Holland classification applied to cases of ductal carcinoma *in situ* (DCIS) of the breast.

Materials and Methods: Forty-three cases of breast lesions diagnosed as DCIS were selected to interobserver analysis. Twelve pathologists received the same set of digitized images from microscopy of the DCIS cases, and answered a questionnaire containing the criteria to compose the modified Black nuclear grading system and Holland classification system. In order to determine interobserver agreement and diagnostic accuracy, a web-based survey was created. It organizes the information collected from each pathologist providing the histological grading of the cases in both classification systems.

Results: The reliability for the modified Black nuclear grade applied to cases of DCIS was acceptable, with Kappa value of 0.23±0.02. Comparing the two classification systems studied, there was a similar agreement among both schemes, showing Kappa value of 0.27±0.03 for the Holland classification. Analyzing a subgroup of pathologists rated according to their interest in breast pathology, a higher diagnostic reproducibility was found for the group of breast pathology experts in relation to the pathology residents only for the modified Black nuclear grading system ($\kappa = 0.43 \pm 0.07$ vs. $\kappa = 0.11 \pm 0.05$; $p = 0.002$). The agreement among all pathologists and the gold standard pathologist similarly followed the results of the interobserver concordance, showing to be acceptable, with Kappa for the overall mode value 0.32±0.10 for both classifications. The findings of Kappa for the mode values among specialists in breast pathology and pathology residents were, respectively, 0.34±0.11 (acceptable) and 0.19±0.08 (weak) for the modified Black nuclear grade and 0.33±0.11 (acceptable) and 0.19±0.08 (weak) for Holland classification.

Conclusions: Breast pathology specialists showed greater reproducibility than pathologists not devoted to this subject for both evaluated classification systems. The diagnostic accuracy was similar for the modified Black nuclear grading system and the Holland's classification system.

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Histopathological Grading of Ductal Carcinoma in Situ of the Breast − Validation of a Web-based Survey Through Intraobserver Reproducibility Analysis

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Background: This study aims to develop a method of systematic application of the diagnostic criteria that compose the histological grades of ductal carcinoma *in situ* (DCIS) of the breast through a questionnaire available in a website, and to determinate its reliability and applicability in clinical practice.

Materials and Methods: The most important criteria to grade DCIS lesions in histopathological bases were selected to compose the point scoring system according to their relevance to three different DCIS classifications. A software was created in order to be accessed through Internet, in website format (http://mayer.art.br/cainsitu/site3). This website offers a questionnaire containing the characteristics used to compose the three DCIS classification systems evaluated in our study, and also the digitized microscopy images of 43 DCIS cases selected. Three pathologists, who are specialists in breast pathology, analyzed the same set of digitized images in this web-based survey. In the first phase, they answered a questionnaire with the characteristics used to compose the modified Black nuclear grade system and the classification systems of Holland and Van Nuys. After at least 6 months, the pathologists read again the same images, but without the help of the questionnaire, indicating subjectively the diagnoses, using the grading system of their daily practice. The intraobserver agreement analysis was used to validate this innovative web-based survey.