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99mTc-sestamibi scintigraphy in axillary lymph node metastases detection in patients with primary breast cancer undergoing curative surgery

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Background: Lymph node status is the primary prognostic discriminant in patients with breast cancer (BC). Although axillary dissection represents the methods of choice for obtaining such information, less invasive staging procedures has been suggested. Preoperative non-surgical techniques include ultrasonography, CT-scan, MRI, 18F-FDG PET, and positive radio-pharmaceutical scintigraphy. The aim of this study was to evaluate the usefulness of 99mTc-sestamibi scintigraphy (SS) in patients with confirmed primary BC undergoing surgery.

Patients and Methods: A series on 159 women (median age 54 years, range 36-78 years) with confirmed primary BC were enrolled in the study. Breast-conserving surgery or mastectomy with axillary dissection was performed in all patients, as indicated by the tumor staging. Once they had given the informed consent, each patients underwent SS. Images were acquired using a single detector gamma-camera equipped with a parallel-hole low-energy high-resolution collimator (256 x 256 matrix, 140 keV energy setting) 10 minutes after 750 MBq radiopharmaceutical I.V. administration, using single-photon emission computed tomography (SPECT) technique. A focal 99mTc-sestamibi uptake and a mass-to-background ratio of more than 1.4 was considered as a positive result in detection of axillary node metastases.

Results: Final pathology showed 33 (20.8%) pT1b, 90 (56.6%) pT1c, and 36 (22.6%) pT2 breast carcinomas. The greatest diameter of the tumor (size) ranged from 8 and 30 mm (median 16 mm). Sixty (37.7%) patients had axillary metastases at surgery (N1), while 99 (60.3%) patients had negative nodes (N0). The average of nodes removed was 19.9±2.1, and the average of positive nodes was 2.7±1.2. The age of the patients significantly correlated with both size (R=0.24, F=9.55, p=0.002) and the number of positive nodes (R=0.33, F=7.11, p=0.0009), and subsequently there was a direct relationship between number of positive nodes and size (R=0.31, F=6.08, p=0.016). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of SS were 81.4%, 91.0%, 84.2%, 91.0%, and 87.4%, respectively. The sensitivity was higher in patients with 3 or more positive nodes (N=27/28, 96.4%), while patients with 2 (N=25) and 1 (N=7) positive nodes the sensitivity was 80.0% and 28.6%, respectively.

Conclusions: 99mTc-sestamibi scintigraphy may be useful in patients undergoing surgery for breast cancer, although its sensitivity is low when the number of involved nodes is two or less. This suggests that others imaging techniques should be used in conjunction with SS when a preoperative assessment of axillary lymph node status is required.

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Role of HER2 in wound-induced breast carcinoma proliferation

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Background: Clinical and experimental data raised the possibility that surgical removal of the primary tumor promotes the growth of metastatic lesions. The aim of the present study was to analyze the impact of surgery on proliferation of breast carcinomas, in particular those overexpressing HER2.

Methods: Proliferation of breast carcinoma cells was evaluated on histological sections of primary breast carcinomas and in residi al tumor found in re-excision specimens, by MIB-1 immunohistochemistry and on in vitro cell lines by a colorimetric assay. EGF-like growth factors were measured by displacement of ¹²⁵I-EGF from its receptor. Cellular damage was measured by creatine phosphokinase level. Down-mo du lation of HER2 was performed by cytoplasmic expression of anti-HER2 antibody and by inhibition with anti-HER2 antibody trastuzumab.

Results: Residi al breast carcinomas surgically-removed within 48 days from a first surgery were found to display a significant increase in proliferation if they were HER2-positive. Accordingly, wound drainages and

post-surgical sera from breast carcinoma patients were found to stimulate the in vitro growth of HER2-overexpressing breast carcinoma cells. Removal of the HER2 oncoprotein from the cell membrane led to a dramatic decrease in the in du ced proliferation. The level of EGF-like growth factors in post-surgical sera, as well as the level of drainage-in du ced proliferation, was directly correlated to the amount of surgical damage evaluated by cpk levels (r=0.77, p=0.002 and r=0.69, p=0.009, respectively). Treatment of HER2-positive tumor cells with trastuzumab, if given before the growth stimulus, abolished drainage-in du ced proliferation.

Conclusions: HER2 overexpression by breast carcinoma cells plays a major role in the post-surgery stimulation of growth of breast carcinoma cells. Partially supported by AIRC.

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High-dose chemotherapy with stem cell support in high-risk primary breast cancer. An analysis of the effect on overall survival the Danish experience from a comparison study

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Background: To analyse retrospectively the effect of high-dose chemotherapy with stem cell support in patients with high-risk primary breast cancer. The effect on overall survival was compared to a control group of patients from the same study period having received conventional therapies.

Material and methods: One hundred and thirty-two patients younger than 55 years and with more than 6 positive axillary lymph nodes and without any signs of metastatic disease received after curative surgery three cycles of inductive chemotherapy by cyclophosphamide, epirubicin and 5-fluorouracil (FEC) in standard-dose. After harvest of peripheral blood stem cells one cycle of high-dose chemotherapy (HDC) including cyclophosphamide, tiotepa and carboplatin (CTCb) was administered. All patients received loco-regional radiotherapy and tamoxifen was administered to patients with estrogen receptor positive tumors. A comparative group of 775 patients with the same prognostic characteristics was identified in the national database and included in the analysis as the control group.

Results: The statistical analysis of the patient materials identified a series of well-known prognostic factors nearly equally distributed in the two treatment groups, only age and number of positive nodes showed some bias. Estrogen receptor (ER) appeared also to be a strong prognostic and predictive variable and should therefore be included in the analysis. The effect of HDC on overall survival is of the same size in patients with ER+ and ER- tumors. The improvement of overall survival by HDC compared to the control group is significant (p=0.045) with a relative risk of death of 0.72 (CI: 0.52-0.9).

A total of 122 patients received FEC as adjuvant therapy. The overall survival of this sub-group compared to the group of 132 having received HDC is slightly inferior but not to a statistical significant level. Two cases of toxic deaths (1.5%) was registered.

Conclusion: We conclude that our analysis of the effect of HDC in relation to the selected comparison group is valid. The effect of HDC on overall survival is significant in comparison to all patients in the control group also when compared to the subgroups with known ER status. However the overall survival of the HDC-group is not significantly superior compared to patients having received FEC as adjuvant therapy. This high-dose regimen is feasible and well tolerated.

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Added value of blue dye in sentinel node biopsy for breast cancer

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Sentinel node biopsy in breast cancer is a new rapidly advancing minimally invasive procedure which enables nodal staging of clinically node negative breast cancer patients without performing complete axillary dissection. There are still controversies over the added value of Blue Dye when lym-