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### Predicting the prognosis of breast carcinoma – What the pathologist should do?

J. Kulka, Sz. Lóth, A.-M. Tóké, C. Kühn, A. Kádár. 2nd Dept. of Pathology, Semmelweis University of Medicine, Budapest, Hungary

**Purpose:** Hundred consecutive cases of invasive breast carcinoma were investigated with special emphasis on the definition of their prognosis using different well established methods.

**Methods:** The tumour size and lymph node status of the WHO's TNM system, the tumour grade using the modified Bloom-Richardson scheme, the Nottingham Prognostic Index (NPI) and an immunohistochemical profile consisting of estrogen- and progesterone receptors, Ki-67 proliferation marker, p53 and c-erbB-2 oncoproteins, of each of the tumours were examined and the results statistically evaluated.

**Results:** Tumour size and lymph node status on its own in this series did not show significant correlation with none of the immunohistochemically investigated prognostic factors. Tumour grade showed correlation with estrogen receptor content and was related to Ki-67 and p53 positivity. As for the NPI, there was a significant correlation with estrogen receptor content, Ki67 and p53 positivity. Neither the grade nor the NPI did show any correlation with c-erbB-2 positivity.

**Conclusion:** It is suggested that NPI be calculated in cases of invasive breast carcinomas because of the ease of its applicability. Its good correlation with biological tumour markers further validates the use of this index in every day practice.

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### Cellbiological factors in relation to nuclear grade and growth pattern

M. Fernö<sup>1</sup>, I. Idvall, C. Andersson, G. Fallén, C. Ingvar, A. Ringberg, C. Strand, M. Åkerman. <sup>1</sup>Dept. of Oncology, University Hospital, Lund, Sweden

The incidence of ductal carcinoma in situ (DCIS) has increased from a few percent to about 20% of all breast cancers after the introduction of mammographic screening. One commonly applied classification system is based on nuclear grade. Andersen and co-workers have stressed the aspect of growth pattern in DCIS, dividing them into microfocal, tumour forming and diffuse DCIS (Andersen *et al.* *Acta Oncol* 27, 739, 1988).

**Purpose:** To study the association between on one hand cellbiological factors [estrogen (ER) and progesterone receptor (PgR), DNA ploidy status, Ki67 (proliferative marker) ERBB2 (oncogene) and p53 (tumour suppressor gene)] and on the other histopathological pattern (nuclear grade and growth pattern).

**Methods:** ER, PgR, ERBB2, p53 and Ki67 were analyzed with immunohistochemical assays and DNA ploidy status with flow cytometry. The histopathological pattern was reevaluated.

**Results:** ER and PgR negativity, ERBB2 and p53 overexpression, high proliferative rate and DNA non-ploidy status were strongly associated with higher nuclear grade ( $p < 0.005$  or less). The associations between these factors and growth pattern according to Andersen and co-workers were weaker, in many cases non-significant.

**Conclusion:** Nuclear grade and growth pattern exhibit different associations to cell biological factors, which suggest that these two histopathological parameters may describe different characteristics of DCIS.

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### Image analysis of imprint cytology from invasive breast carcinoma and its relation to axillary node metastasis

I. Idvall<sup>1</sup>, L. Ingvaldsson<sup>1</sup>, Y. Knutsson<sup>1</sup>, T. Lindén<sup>1</sup>, M. Fernö<sup>2</sup>. <sup>1</sup>Department of Pathology/Cytology; <sup>2</sup>Department of Oncology, University Hospital, 221 85 Lund, Sweden

For small breast carcinomas  $\leq 10$  cm partial mastectomy without axillary exeresis is discussed. Also in breast carcinomas  $> 10$  mm probably axillary exeresis can be avoided based on the status of the sentinel node. The histopathological processing of the sentinel node is, however, time-consuming and a definite diagnosis cannot be established the operation day.

**Purpose:** To investigate the association between image analysis of nuclear area of invasive breast carcinomas and axillary node status.

**Method:** Imprints from 97 cases of invasive breast carcinomas  $> 10$  mm diameter, were fixed in 95% ethanol, stained with hematoxylin-erythrosin

and nuclear area determined by image analysis. 100 tumor cells were analysed.

**Results:** 24 breast carcinomas with mean nuclear area  $\leq 60 \mu\text{m}^2$  and only  $\leq 5\%$  tumor cells  $> 100 \mu\text{m}^2$  had no axillary lymph node metastasis. Remaining breast carcinomas had mean nuclear area varying between 62 and  $135 \mu\text{m}^2$  and  $> 5\%$  tumor cells measuring  $> 100 \mu\text{m}^2$ ; 42 were node negative and 31 node positive.

**Conclusion:** If this method can be applied to fine needle aspiration cytology it is possible to separate one group of invasive breast carcinoma, where the surgical procedure of sentinel node can be avoided.

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### Nuclear abnormalities (nuclear pockets) in apocrine breast carcinoma: Report of a case

P. Stravoravdi, A.N. Grekou, P. Patakiouta, T. Tsoukalas, Th. Toliou, K. Dimitriadis. (Techn. P. Oustambasidis), "Theagenio" Cancer Hospital of Thessaloniki, Greece

**Purpose:** The existence of nuclear pockets, which represent nuclear abnormalities, has been recently mainly described in a variety of leukemias and lymphomas. We, herein, report the detection of nuclear pockets in a case of breast carcinoma.

**Case Report:** Our case involves a grade III infiltrating ductal carcinoma of apocrine type, with an extensive in situ component, in a 60 year old woman. Specimens for ultrastructural analysis were routinely processed, stained with uranyl acetate and lead citrate and examined with the electron microscope.

**Results:** We observed the characteristic nuclear pockets in many carcinoma cells. Mostly, these pockets contained cytoplasm of the same composition as the perinuclear cytoplasm. Some pockets, however, contained intranuclear material. The most impressive finding was the occasionally coexistence of nuclear pockets together with helioid inclusions, which are also rare nuclear inclusions.

**Conclusions:** Nuclear pockets and even more nuclear pockets together with intranuclear helioid inclusions have not been previously described in breast carcinoma. These irregularities may indicate increased nucleo-cytoplasmic exchange in parallel with increased nuclear surface area. The precise functional significance of nuclear pockets is uncertain. Since their presence is generally correlated with poor prognosis, their role in breast cancer remains to be elucidated.

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### Adenoid cystic carcinoma of the breast: About 14 new cases

G. Vlastos, P. Validire, K.B. Clough. Institut Curie, Paris, France

Adenoid cystic carcinoma of the breast (cylindroma) is a rare neoplasm accounting to fewer than 0.1% of all breast carcinomas. Less than 200 cases are reported.

**Aims:** To review 14 new cases and give recommendations regarding prognosis and treatment of this carcinoma.

**Materiel and Method:** 14 cases have been identified in a 15 years review of 14,000 cases of breast cancer treated at the Curie Institute, Paris.

**Results:** Mean age is 61 years old (age distribution 34 to 80). The most frequent presenting symptom is tumor (78.5%) with no predilection either the left or the right breast. Preoperative cytology is useful in 35% of cases. Characteristic microscopic appearance of adenoid cystic carcinoma, featuring a mixture of glandular (adenoid component) and stromal or basement membrane material (cystic, pseudoglandular or cylindromatous component) are found. Axillary metastasis is rare (1 case). Treatment options are various. Surgery is performed in 78% of these cases: 3 local excisions, 5 with axillary dissection and 2 radical mastectomies. Radiotherapy is the treatment of choice for 3 women. A combined treatment is reported in 6 cases. Local recurrence occurs in 2 cases; pulmonary metastasis in only one. Follow-up ranged from one month to 14 years, with 4 deaths reported.

**Conclusion:** These datas suggest that prognosis of adenoid cystic carcinomas is favorable; axillary and distant metastasis are rare. Breast conserving treatment may be applicable in most cases.