

evaluate the prognostic value in addition to clinicopathological parameters and patient survival.

Methods: In this retrospective study formalin fixed and paraffin embedded tissue specimen of 75 patients with breast cancer were immunohistochemically stained. Specific anti-E-cad monoclonal antibody, HECD-1, and anti-K18-antibody, CK2, were used. The staining intensity was compared with clinico-pathological values and follow-up datas spanning 80 months.

Results: A definitive positive staining was observed in 21 (28%) specimens for E-cad and 15 (20%) specimens for K18. The survival rate in the E-cad-positive group (81%) and in the K18-positive group (93%) was much higher than in the E-cad-negative or K18-negative groups (both 48%). E-cad and K18 were independent from each other and independent from lymph node status, tumor size/grading and estrogen status. The relative risk to die due to breast cancer within 80 months was decreased in groups positive for K18 (0.08), E-cad (0.28), and ER (0.49). A positive lymph node status increased the relative risk (3.66).

Conclusion: These results suggest that E-cad and K18-expression can serve as independent prognostic indicators for the invasive potential of breast cancer.

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PUBLICATION

Immunohistochemical studies on oncogene products (C-erbB-2) and p53 protein in human breast cancer: Is it significant for tumor evolution?

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Purpose: The prognostic value of membranal C-erbB-2 oncoprotein and p53 protein was determined in a study of 93 cases of breast tumors surgically removed. For a correct evaluation the relationship between these markers and tumor size, histological and malignancy grade and lymph node metastases was done.

Methods: 93 patients with different stages and types of breast carcinomas were analysed immunohistochemically with specific antibodies on paraffin-embedded material, for both c-erbB-2 and p53 proteins on serial sections of 4 µm. C-erbB-2 staining was rated by counting the number of positive cells and the intensity of the reaction. The markage with MoAb for p53 overexpression was established by numbering the stained nuclei. We used MoAb Do-7 Dako, Denmark for p53 and anti c-erb B-2 oncogene protein from Boehringer-Mannheim.

Results: C-erbB-2 oncoprotein was overexpressed in 74 cases and p53 protein in 80 cases. C-erbB-2 is more specifically an early factor for poor prognosis while p53 proteins overexpression is a long term factor poor prognosis.

Conclusions: The simultaneous determination of c-erbB-2 oncoprotein and overexpression of p53 protein seems to have a prognostic significance for breast cancer patients. We consider that is of much interest to focus the studies for small-size tumors and the axillary lymph node status. The membrane c-erbB-2 level seems to be an important independent prediction for the prognosis.

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PUBLICATION

Possible causes of breast cancer in women working at coke-chemical factory (CCF)

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Purpose: Unfavorable influence on reproductive system of factors associated with coke-chemical manufacture is well known. We studied risk factors for breast cancer in women working at CCF.

Methods: Mammologic and general examination of 1379 women working at CCF with age range from 20 to 54 years was performed. Women with breast cancer and women from control group underwent extended examination including assessment of hormonal and immune status.

Results: Breast cancer was revealed in 3 cases. Women with breast cancer were found to have significantly more risk factors compared with control (15.9 + 10.6 versus 14.8 + 6.1, p < 0.05) according to WHO's 56 criteria of breast cancer risk, proposed in 1984. These women had worked in principal workshops for 10–15 years and had reproductive age. Most important factors were a high fat diet and vitamin deficient diet, somatic pathology – obesity, hypertension, hepatocholecystitis and neuro-endocrine syndromes. No one had first degree relatives with cancer. Two women had A (II) blood group. One woman had hyperprolactinemia (785 mU/l) with

relative hyperestrogenemia. All women with breast cancer had decreased amount of T-cells (CD3+) – 61.10 + 0.51 versus 72.10 + 4.40 (p < 0.01) and IgA antibodies – 2.68 + 0.24 versus 4.62 + 0.90 (p < 0.05).

Conclusion: For development of breast cancer were found to be important length of service at CCF and background disturbances of health most prominent in hormonal and immune systems.

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PUBLICATION

Determination of fibrin D-dimers in patients with breast cancer after cytotoxic chemotherapy

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Purpose: The biologic behaviour of cancer cells relates to tumor burden, tumor invasiveness as well as some factors of the fibrinolytic pathway.

Methods: The aim of the present study was to monitor changes in the serum levels of fibrin D-dimers in patients with breast cancer undergoing cytotoxic chemotherapy separated into two groups; group A: patients receiving adjuvant chemotherapy and group B: patients undergoing chemotherapy with advanced/metastatic disease. D-dimers were determined with the Latex method (Diagnostica Stago); normal values: <0.5 µg/ml.

Results: Elevated D-dimer values were found in 4/20 (20%) patients in group A (range: 5–36 µg/ml) and in 14/20 (70%) patients in group B (range: 11–102 µg/ml) (P < 0.01) before the initiation of chemotherapy. The study is ongoing and further patient accrual is in progress and data will be presented regarding changes in D-dimer serum levels during or after cytotoxic chemotherapy. In particular, interest should be given to patients receiving adjuvant chemotherapy and show elevation of D-dimer levels.

Conclusion: Serum D-dimer levels may prove to constitute an important prognostic factor in patients with breast cancer receiving chemotherapy in the adjuvant setting or for advanced/metastatic disease.

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PUBLICATION

Prognostic value of cathepsin D in breast cancer (BC) patients

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Purpose: to assess the prognostic value of cathepsin D quantification on tumour cytosols as a biological marker in BC patients.

Pts and Methods: 147 pts with primary BC were selected for study; median follow-up was 5 yrs. Mean age 59 yrs (range 25–88); postmenopausal 72%; T1: 32%; T2: 44%; T3–T4: 24%. N0: 45%; N1–3: 26%; N > 4: 29%. Histologic type: ductal Ca: 88%; Lobular Ca: 8%; histologic grade SBR1: 7%; SBR2: 59%; SBR3: 34%. Cathepsin D was quantified on tumour cytosols by CIS radioimmunoassay. Results were compared according to pt and tumour characteristics.

Results: Mean cathepsin D value was 70 pmol/mg cytosolic prot. (range 0–706). With regard to pt and tumour characteristics, cathepsin D mean level was higher in premenopausal women (p = 0.007). Tumour size, nodal invasion and hormone-receptor status were the main prognostic factors for disease free (DFS) and overall survival (OS). 1.5-year OS was 70% and DFS was 58%. In multivariate analyses, DFS and OS were shorter for cathepsin D levels >30 pmol/mg prot (p = 0.01) and (p = 0.04) respectively.

Conclusion: in our series, cathepsin D levels >30 pmol/mg prot is an independent factor for DFS and OS in breast cancer patients.

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PUBLICATION

Influence of prognostic factors on overall and disease free survival in male patients with primary carcinoma of the breast

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Purpose: To determine the value of prognostic factors (age, stage of disease, extent of lymph node involvement, histological grading and hormone receptor status) in male patients.

Patients and Methods: In 31 male patients (mean age 65.7 years, SD ± 11.5) with breast cancer therapy regimen included postoperative

radiotherapy of the chest wall as well as additional hormone therapy ($n = 8$) and/or chemotherapy ($n = 3$). Tumor distribution by stage was as follows: stage 0 (9.7%), stage I (22.6%), stage II (32.2%) and stage III (35.5%). Histopathologic study revealed invasive ductal carcinoma in 27 pts, 1 invasive lobular carcinoma and 3 ductal carcinoma in situ.

Results: The mean follow-up was 77.6 months (range, 7.3–231.8). Only one in-field local relapse was observed. Eight patients (25.8%) experienced metastatic tumor spread, in 7 patients (22.6%) a second malignancy was observed. Kaplan-Meier estimates of OS and DFS at 5 years were 77% (95%CI, 0.61–0.93) and 73% (CI, 0.57–0.91), respectively. Risk factors that reached statistical significance on DFS in the Cox regression model were stage of disease ($p = 0.020$), lymph node involvement ($p = 0.026$) and histopathological grading ($p = 0.017$). None of the prognostic factors were found to be of statistical value for OS.

Conclusion: Stage of disease, lymph node involvement and histological differentiation are of prognostic impact on disease free survival.

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PUBLICATION

Male breast cancer – New prognostic factors?

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Purpose: Male breast cancer (MBC) is a rare disease and this explains our little knowledge in prognosis. Research around MBC is inspired in findings for this cancer in females. In a population of patients with histologically confirmed MBC, known in its clinical characteristics, we purposed to test the expression of the v6 isoform of CD44 protein and its impact in prognosis.

Population and Methods: For MBC patients treated in our institution we review the main clinical characteristics with a possible effect in prognosis and their survival patterns. In the biopsy tissue we checked the immuno-expression of CD44v6 protein. The statistical analysis focus was to find relations between classical clinical and pathological variables and the CD44v6 expression, in order to define the contribution of this new factor for survival in the context of MBC.

Results: We tested CD44v6 protein in 31 cases of MBC. In 19 (59%) it was positive. A significant difference between expression of CD44v6 and histological grade was found with a greater percent of expression in undifferentiated tumors ($p = 0.03$). In tumors with positive estrogens receptors we found a greater expression of CD44v6 ($p = 0.03$). The CD44v6 expression in 16 lymph nodes with tumor invasion was positive in 9, with some of discordance between expression of CD44v6 in the primary tumor and in lymph node metastases, in one case only the lymph node was positive for CD44v6, in 4 cases the lymph nodes metastases had a greater expression than the primary. There was no difference in survival between the two groups, with and without expression of CD44v6.

Conclusions: The expression of CD44v6 in our group of patients with MBC is similar to that found by other authors in female breast cancer. It seems that CD44v6 expression is present in more aggressive tumors and, although without statistical significance, associated with a worse survival and shorter disease free survival. Lymph node expression for CD44v6 is occasionally higher than in the primary tumor. Our results support the ongoing research for new prognostic factors in MBC, being necessary larger series of patients in order to identify independent prognostic factors.

with the "Talon" system for cranial sites or an acquaplast mask. Target volumes up to 500 cm³ have been treated. Multiple lesions (up to 3) were treated in one set-up. The range of dose/fractionation schemes used was 15Gy/1f–70Gy/35f. Dose validation was carried out using film and TLD dosimetry.

Results: Optimal dose distributions were attainable using inverse treatment planning for IMRT delivery. These were found to encompass the target volumes accurately using dose validation phantom studies. Immobilisation methods used were accurate to within 2 mm as evidenced by weekly portal films.

Conclusion: IMRT using the Peacock system offers the advantages of delivery of conformal therapy to high doses safely and accurately. This provides the opportunity for dose escalation studies, re-treatment of previously treated tumours as well as treating multiple targets in one set-up. The system may be fitted to a conventional linac without major modifications.

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ORAL

Stereotactic radiotherapy in the treatment of ocular melanoma

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Introduction: Ocular melanoma is frequently treated by the interstitial implantation of 198Au seeds, by the application of 60Co plaques or 184Ta wire, by external beam radiotherapy using small 60Co beams or by proton therapy. The last technique, though very expensive, provides improved dose distributions and dose localizations in the treatment of tumours adjacent to critical normal tissues, thereby allowing dose prescriptions as high as 70 Gy in 5 fractions over 8–9 days.

Purpose: The technique of stereotactic radiotherapy on a linear accelerator is being used successfully in treating various sites in the brain such as craniopharyngioma, glioblastoma, meningioma, pituitary adenoma, etc. It combines stereotactic localization with fractionated dose delivery. It has now become possible to extend the technique to the treatment of ocular melanoma using the same fractionation scheme as in proton therapy but at a considerably lower cost.

Methods: Stereotactic radiotherapy treatments are delivered using the Radionics' couch mounted system on a Varian 2100C/D linear accelerator and 6 MV photons. The relocatable Gill-Thomas-Cosman (GTC) frame, with an eye fixation device developed here, is attached directly to the dental plate assembly. Treatment planning is accomplished by the new XKnife-4 software. Circular fields between 10 mm and 20 mm diameter with five arcs and a prescription of 70 Gy in 5 fractions over 10 days have been commonly used for treating five patients so far.

Results: The technique developed at the Princess Margaret Hospital for the treatment of ocular melanoma has yielded excellent localization and dose distributions.

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ORAL

Proton radiation therapy (PRT) for pediatric optic pathway gliomas: Comparison with 3D planned photon and a standard photon technique

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Purpose: We compared PRT and its normal tissue (NT) sparing with two photon radiation treatment techniques for localized and extensive optic pathway tumors.

Methods: Based on CT data sets of 7 children, previously treated with PRT, we computed 3D photon and lateral photon plans using the same treatment planning software. Radiation exposure for NT and discrete organs at risk was quantified.

Results: Analysis for small (<20 cm³) and larger (>80 cm³) tumors showed that protons encompassed the smallest volumes of NT at all isodose levels. Comparable conformity and high dose gradient were achieved for protons and 3D photons in small tumors. However, differences became larger with increasing tumor volume and complexity. At low isodose levels 3D photons encompassed the highest amount of NT. PRT reduced doses to the contralateral optic nerve by 48% and 77% compared to 3D photons and lateral photons, respectively. Dose reductions with PRT were 11% and 16% for the chiasm, 13% and 16% for the pituitary gland, and 39% and 54% for the temporal lobes.

Radiotherapy techniques

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ORAL

Tomotherapy with peacock: The University of California, Irvine experience

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Purpose: Intensity modulated radiotherapy (IMRT) offers unique advantages in radiation treatment planning and delivery. In this work, our experience using the NOMOS Peacock system for IMRT is summarised.

Methods: Dosimetric data were acquired to commission the system for clinical use. To date, 80 patients were treated using this system which is fitted to a Clinac 600C linac. Cranial as well as extracranial lesions have been treated using this modality. Immobilisation is achieved either