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The polymorphic enzymes *N*-acetyltransferase 2 and glutathione *S*-transferase M1 in bladder cancer patients

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Purpose: Shifts of *N*-acetyltransferase 2 (NAT2) and glutathione *S*-transferase M1 (GSTM1) which are involved in metabolism of carcinogenic aromatic amines and polycyclic aromatic hydrocarbons (PAH) resp. were to investigate.

Methods: 179 bladder cancer in-patients were interviewed for possible bladder cancer risk factors. All patients were phenotyped for NAT2 by HPLC using molar ratios of urinary caffeine metabolites. A subgroup of 89 patients was genotyped for GSTM1 by PCR of lymphocyte DNA.

Results: 64% of the 179 bladder cancer patients had a low acetylating capacity ("slow" acetylators). In 70% of the 89 genotyped bladder cancer patients GSTM1 gene was lacking. The distribution of NAT2 and GSTM1 in office personnel (59% slow acetylators, 54% GSTM1 negative) did not differ from normal population. Slow acetylators were overrepresentated in smokers (72%), occupationally exposed to colorants (71%) and in coke oven workers (5 out of 6). 16 out of 19 coal miners (84%), 10 of 13 exposed against fumes (77%), 5 of 8 exposed against tar and all four genotyped coke oven workers were GSTM1 negative.

Conclusion: The results are consistent with the view that "slow" acetylator status and the lacking of GSTM1 gene are genetically determined risk factors for bladder cancer in persons exposed to aromatic amines and PAH.

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High precision conformal radiotherapy (RT) (HP-CRT) of patients with prostatic cancer

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Purpose: Biopsies two years after RT-treatment for prostate cancer indicates remaining tumour cells in 20–60% of biopsies. Higher doses (>70 Gy) with large fields increases the risk for serious side-effects Due to day-to-day set-up variation and movement of the prostate, a margin of less than 1.5–2 cm is always inaccurate since it might miss the tumour. Visualisation of the prostate on the treatment machine has not been possible. New technical improvements are needed to accurately localise the prostate during RT.

Methods: We have developed a new technique to accurately position the prostate during RT. The method only needs a simple fixation set up. The technique is used clinically during CT planning, field simulation and when RT is delivered.

Results: With this new treatment technique the day to day variation is this less than ±1 mm. The technique has been tested on 7 patients with conventional dose level (70 Gy) and 15 patients in the first Scandinavian dose escalation study with external beam radiotherapy. Side effects are evaluated weekly by the doctor (according to EORTC/RTOG) and by the patient with a daily diary and a self assessment questionnaire (QUFW-94). The new technique will be presented together with evaluation of side-effects.

Conclusion: With the new HP-CRT we have developed a technique that allows us to increase the dose to the prostate without excessive side-effects. The need of margin will decrease from 1.5–2 cm down to 1–2 mm.

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Results of conformal radiotherapy in prostate cancer

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Purpose: Results of conformal radiotherapy in prostate cancer were evaluated in terms of toxicity, local control, biochemical control and survival.

Methods: From January 1992 to June 1995 curative radiotherapy was planned with a 3D-system in 52 patients. 45 patients were treated for primary tumor and 7 patients for local recurrence. 34 patients received hormonal treatment additionally. The prostate was irradiated with total doses up to 70 Gy, dose per fraction of 1.8–2.0 Gy, 5 f./w.. Individual risks were estimated by dose volume histograms for normal tissues.

Results: The mean follow-up is 32 months. Actuarial local control, biochemical (PSA) control and survival are 95% (3 Yrs.). There were no severe acute or late effects. Only two local recurrences occurred.

Conclusions: Conformal radiotherapy is a safe and an effective treatment for patients with localized carcinoma of the prostate.

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Prostate cancer below 60 years of age: Increasing incidence and worsening prognosis?

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Purpose: Increased awareness of prostate cancer and improved diagnostic techniques have led to earlier and increased detection resulting in improved overall prognosis, mainly in elderly patients. We investigated if improvement of prognosis has also occurred in young prostate cancer patients.

Methods: European standardized incidence rates and relative survival rates were calculated for patients aged 40–59, diagnosed and registered in the cancer registries of Southeastern Netherlands and East Anglia, UK.

Results: The incidence increased by 42% in the Netherlands and by 66% in East Anglia. The 5-year relative survival rate declined from 65% in 1975–1979 to 48% in 1985–1989 in Southeastern Netherlands and remained largely unchanged in East Anglia. The proportion poorly differentiated tumours increased from 15 to 25% in Southeastern Netherlands.

Conclusion: The unfavourable trends in prognosis are remarkable because an improvement would have been more plausible. Similar findings from other European countries suggest an increasing risk of lethal prostate cancer at young age.

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P53 nuclear reactivity and the prognosis and response to chemotherapy in patients with metastatic bladder cancer

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Purpose: We investigated the relationship between p53 nuclear immunoreactivity in bladder tumors and the response and outcome following chemotherapy in patients with metastatic bladder cancer.

Methods: Fifty patients with metastatic bladder cancer were evaluated by P53 nuclear reactivity. Immunohistochemical analysis of P53 nuclear reactivity was detected by PaO 1801 in archival paraffin embedded tissue sections from primary tumor. The patients received combination chemotherapy including cisplatin, methotrexate, together with either carboplatin or doxorubicin and vinblastine.

Results: Twenty-four patients had tumors with a positive reaction to P53. The median survival after chemotherapy was 5.9 months and the overall response rate was 38%. The survival of the patients, with a positive P53 reactivity was 8.4 months, whereas patients without reactivity survived 5.2 months ($P = 0.38$). Response to chemotherapy was achieved in 50% of patients with P53 positive tumors compared to 27% of the patients with P53 negative tumors ($P = 0.14$).

Conclusion: Patients with P53 positive tumors can respond to chemotherapy, allowing adjuvant treatment to be considered in these patients.

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Fluorescent and immunocytochemical stainings of primary urine derived cell cultures from patients with TCC

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Purpose: For successful treatment of TCC, early diagnosis by non-invasive means is important. Sensitivity of conventional cytology is limited. We reported that (Jpn. J. Cancer Res, 87; 718–23, 1996) p53 IMC is useful for early detection and intensive follow-up of patients with TCC. To develop more sensitive methods, we further analyzed p53, mdm2 IMC and acridine orange (AO) fluorescent stainings of primary urine derived cell cultures.

Methods: p53 and mdm2 IMC was performed in 20 patients and 20 healthy controls. AO fluorescent staining was performed in 26 patients, and 23 healthy controls, divided in two step.