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## Risk estimation for side effects of radiotherapy in patients with prostate cancer

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**Purpose:** We have evaluated the impact of 3D-treatment planning and dose-volume-histograms (DVH) on frequency and grade of side effects in patients undergoing definitive radiotherapy for prostate cancer.

**Methods:** 25 patients (group 1) with prostate cancer T1-3N0 underwent conventional radiotherapy from 6/89 through 4/94. The total dose to the prostate was 58–62 Gy with single doses of 1.5 Gy (including pelvic lymph nodes up to a dose of 49.5 Gy) or 2 Gy (for irradiation of the prostate only). All patients had individually collimated fields. This group was compared to a group of 10 patients who received 3D-treatment from 1/96 through 8/96. The total dose in the latter group ranged from 64 to 70 Gy with single doses of 1.8–2.0 Gy.

**Results:** All patients with conventional treatment had acute side effects of rectum and/or bladder grade II–III, grade IV complications were not observed. In patients with 3D-treatment, the maximum acute side effects were grade 1 or less. All 3D-patients had favourable DVH (low risk group according to Hartford et al., Int. J. Radiat. Oncol. Biol. Phys. 1996). Two patients in group 1 have developed chronic sequelae (1 chronic proctitis, 1 anal fissur). Out of patients in group 2, none has developed late sequelae up to now.

**Conclusions:** Patients treated with 3D-conformal radiotherapy for prostate cancer have a low risk for acute side effects with a total radiation dose up to 70 Gy. The use of DVHs helps to optimize dose distribution in critical areas with regard to the NTCP-concept.

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## 'Cancer – testis' antigen-expression in prostate carcinoma

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Several tumor-associated antigens have been described in tumors of different origin, that can be recognized by cytolytic T-lymphocytes and/or antibodies. A group of antigens, first characterized in human melanoma, comprises antigens that are expressed in different tumors, but not in normal tissues except testis, therefore designated as 'cancer-testis' antigens. In the present study we analyzed 59 samples of prostate cancer tissue for the expression of CTL-defined 'cancer-testis' antigens such as MAGE-1, MAGE-2, MAGE-3, GAGE and for antibody-defined antigens such as HOMMEL-40 and ESO-1, also showing the 'cancer-testis' pattern of expression. About 15% (9/59) of prostate cancer tissues expressed at least one of the 'cancer-testis' antigens tested. Of these, 4/9 showed co-expression of at least two of the antigens evaluated. The expression of antigens seems to be heterogenous with respect to different metastatic sites. All tumor samples that typed positive for CTL-defined antigens were obtained from hormone refractory metastatic disease. Our findings suggest that CTL-defined 'cancer-testis' antigens expressed by prostate carcinomas may represent attractive targets for peptide-based immunotherapy for this disease. The potential diagnostic and therapeutic significance of antibody-defined antigens expressed by prostate cancer remains to be determined.

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## Early outcome of radiation treatment for clinically-localised prostate cancer

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Patients with radically irradiated prostatic carcinoma were reviewed to assess early morbidity and early treatment efficacy in a newly established radiation oncology unit. Outcomes for 130 patients treated with radical external-beam irradiation for localised prostate carcinoma from September 1993 to March 1996 were retrospectively analysed. All patients were treated with a consistent technique. Pretreatment, acute, and late toxicity were assessed and biochemical-relapse-free and clinical-relapse-free survivals were recorded. Possible prognostic variables for all of these endpoints were investigated. The median age was 70 years. The "T" classification of the primary tumours were as follows: T1 14%, T2 51%, T3 34% and T4 1%. 9% of patients had well-differentiated tumours, 75% moderately-well differentiated tumours, and 17% had poorly-differentiated tumours. The median recorded PSA at presentation was 12.2 ng/mL. Of the patients, 46% experienced grade 1 acute bowel toxicity, 45% grade 2 and 1% grade 3, while for acute bladder there were 61% with grade 1, 24% grade 2, and 4% with grade 3 toxicity. 37% of patients experienced grade 1 late bowel morbidity, and 10% of patients grade 2, while for late bladder toxicity, 23% of patients with grade 1.5% with grade 2 and a single patient with grade 3 were observed. Variables were evaluated for possible influence on acute and late morbidity, but none of these were found to be statistically significant. Ten patients had "biochemical" disease progression. Five patients experienced "clinical" progression. In conclusion, very few patients suffered moderate or severe treatment morbidity. The higher rate of biochemical progression, compared with clinical relapse, is consistent with published data.

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## Docetaxel and cisplatin (DC) combination chemotherapy for metastatic urothelial cancer

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**Purpose:** Docetaxel is a taxane derivative with encouraging single agent activity in the treatment of metastatic urothelial cancer. We combined this agent with cisplatin and performed a phase II study.

**Methods:** Between 3/1996 and 1/1997, 27 patients (pts) with measurable metastatic disease originating from the bladder (22 pts) or the upper urothelial tract (5 pts) and no prior metastatic chemotherapy were treated with DC as follows: Docetaxel 75 mg/m$^2$ one hour IV infusion and cisplatin 75 mg/m2 IV on day 1, plus G-CSF from days 5 to neutrophil count recovery. The treatment was given on an outpatient basis and courses were repeated every 3 weeks for a maximum of 6 cycles.

**Results:** Pts' median age was 68 years (range 44 to 79), median PS was 1 (range 0 to 3). 7 patients had previously received XRT and 9 were treated with adjuvant or neoadjuvant MVAC chemotherapy. Grade 3 or 4 toxicities (WHO): neutropenia 9 pts (4 pts developed neutropenic fever), anemia 4 pts, diarrhea 4 pts, nausea and vomiting 2 pts, mucositis 1 pt; no treatment related mortality. 24 pts have already completed 3 courses and are evaluable for response, the objective response rate so far is 58% including 4 pts who achieved CR and 10 pts PR.

**Conclusion:** The DC regimen is active in pts with metastatic urothelial cancer and poor disease features (older age, prior XRT, prior upadjuvant or adjuvant chemotherapy) and requires prospective comparison with other active regimens.

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## Osteoblastic metastases: Metabolic and morphologic aspects

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**Purpose:** In order to verify the subtle morphology of osteoblastic metastases by non-invasive methods, one possibility is to measure the markers which are known to be highly sensitive and specific for bone turnover. In this study we compared the levels of bone markers with the bone histological pictures of 82 patients (pts) with prostatic cancer and osteoblastic metastases.

**Methods:** Measurements were made of blood calcium (Ca), phosphate ($PO_4$), alkaline phosphatase (Alk. Ph.) levels and bone Gla protein (BGP); 24-hour urine specimens were assayed to determine calcium (UCa), phosphate ($UPO_4$) and hydroxyproline (UHOP) levels. 24 h whole body retention (WBR%) of $^{99m}$Tc-MDP was also measured. Histological analyses of the bone metastases were made using transiliac bone biopsy specimens.

**Results:** Alk. Ph., BGP and WBR levels were above normal limits in respectively 80%, 88% and 82% of the pts; UCa and $UPO_4$ levels were below normal limits in respectively 42% and 64% of the pts; and UHOP levels were high in 51%. The 82 pts were subdivided into two groups: the first consisted of 34 pts with urinary calcium levels below the norm; the second of 48 pts with normal levels. The bone biopsies taken from the pts in the first group showed a prevalently osteosclerotic component, whereas those taken from the pts in the second group revealed a prevalently osteolytic component.

**Conclusion:** These results suggest that the measurement of bone turnover parameters is useful in assessing the effective osteolytic component of apparently sclerotic metastases.