toxicity for white blood cells (2 cases), for hemoglobin (1 case) and for platelets (1 case). 19 patients have been evaluated endoscopically so far. CR were observed in 11/18. No case of progression was observed.

Conclusions: Intravesical gemcitabine at the dose of 2000 mg weekly for 6 weeks has an effective ablative action on papillary marker lesions from intermediate risk superficial bladder cancers. Side effects are mild. No significant hematological toxicity has been recorded in our series.

860 POSTER

Proton therapy for invasive bladder cancer: Treatment results of a bladder-preserving therapy with x-ray irradiation and concurrent intra-arterial chemotherapy followed by proton irradiation boost

M. Hata[1], N. Miyanaga[2], K. Tokuuye[1], K. Ohara[1], Y. Saida[3], S. Sugahara[1], K. Kagei[1], T. Hashimoto[1], H. Akaza[2], Y. Akine[1]. *[1] University of Tsukuba, Radiation Oncology, Tsukuba, Japan; [2] University of Tsukuba, Urology, Tsukuba, Japan; [3] University of Tsukuba, Radiology, Tsukuba, Japan*

Background: In the treatment of invasive bladder cancer, proton beam irradiation having an excellent dose localization to the target may contribute to formulating a treatment regimen with less morbidity and more efficacy in both local tumor control and bladder preservation. We present results of treatments for 23 patients with invasive bladder cancer treated with x-ray irradiation and concurrent intra-arterial chemotherapy followed by proton boost to the primary site.

Material and Methods: Twenty five patients with transitional cell carcinoma of the urinary bladder, cT2-3N0M0, were entered in the present study. All patients underwent transurethral resection of the bladder tumor(s) followed by x-ray irradiation (41.4 Gy in 25 fractions with 10-MV photons) to the small pelvis and concurrent intra-arterial chemotherapy (methotrexate 30 mg/m^2 and cisplatin 50 mg/m^2, 3 courses at 3-week intervals). Upon completion of the treatments, the patients were evaluated with transurethral observation and biopsy. When a patient had no residual tumor, he/she received a boost dose (33 Gy in 11 fractions) with proton beams to the primary sites. When a patient had a residual tumor, he/she underwent radical cystectomy.

Results: Twenty-three of the 25 patients (92%) had no residual tumor at the time of tumor re-evaluation, and hence received proton therapy. The remaining two patients having residual tumors underwent radical cystectomy. Of the 23 patients treated with proton therapy, nine had recurrences; local recurrences in six patients, distant metastases in two and both in one. All local recurrences were controlled with salvage therapies and all of the three patients with distant metastases died of cancer. The 5-year over-all, disease-free and cause-specific survival rates were 61%, 65% and 84%, respectively. The 5-year local tumor control and bladder-preservation rates were 73% and 100%, respectively. It was found by the multivariate analysis that T category and the number of tumors were the significant prognostic factors for the survival ($P<0.01$) and for the local tumor control ($P< 0.05$), respectively. Treatment toxicities of grade 3-4 were found in eight patients; hematologic toxicities in six patients and hemorrhagic cystitis in two.

Conclusions: The present regimen of bladder-preserving therapy for invasive bladder cancer was feasible and effective. Proton therapy contributed significantly in improving local tumor control and bladder preservation.

861 POSTER

Risk-adapted brachytherapy of prostate cancer using J - 125 permanent implantation

P.M. Messer[1], H.-W. Gottfried[2], N.M. Blumstein[3], E. Schneider[1], E.M. Röttinger[1]. *[1] Ulm University, Department of Radiation Oncology, Ulm, Germany; [2] Ulm University, Department of Urology, Ulm, Germany; [3] Ulm University, Department of Nuclear Medicine, Ulm, Germany*

Background: To examine causes of early biochemical recurrence after permanent brachytherapy. Risk factors and therapeutic consequences are worked out.

Materials and methods: After a median time of 14 months four of 112 patients developed biochemical progress. Post planning dosimetry at four weeks after implantation showed a median D 90 of 151,5 Gy (144,8 - 159,3 Gy). Restaging using ^{11}C-Cholin-PET/CT unveiled an isolated relapse in the seminal vesicles. Patients' records were reviewed to figure out common factors. Recurrences to the seminal vesicles were histological proven.

Results: All patients with recurrences had initially histological positive specimen from the base and or mid of the prostate and a PSA between 5 and 10 ng/ml. Depending on these results, we decided to include in these patients the seminal vesicles into the target volume. Up to now 9 patients with the above defined risk factors were treated with permanent brachytherapy according to this regime. Post planning dosimetry showed a minimal dose of 148 Gy in the area of the seminal vesicles. During follow up no change in the acute and late side effects was observed compared to patients receiving brachytherapy to the prostate only.

Conclusion: In patients with histological positive specimen from the base of the prostate should be included into the treatment volume. In addition ^{11}C-Cholin-PET/CT has been included into the staging procedures prior to treatment.

862 POSTER

Evaluation of a superantigen- mediated immune response as therapy for superficial bladder cancer.

P.L. Willert[1], F.G.E. Perabo[1], D.H. Schmidt[1], M. Sitzia[1], E. Wardelmann[2], A. Von Rücker[3], A. Wirger[4], P. Albers[1], S.C. Müller[1]. *[1] University Hospital, Dept. of Urology, Bonn, Germany; [2] University Hospital, Institute of Pathology, Bonn, Germany; [3] University Hospital, Institute of Clinical Biochemistry, Bonn, Germany; [4] Medical University, Dept. of Urology, Luebeck, Germany*

Background: Potent activators of T lymphocytes are toxins produced by Staphylococcus aureus. The characteristics of these Superantigens can be exploited in diseases where strong immunologic responses are required. We initiated this study to evaluate a new approach in an immunomodulating intravesical therapy of superficial bladder cancer.

Material and Methods: We first examined by flowcytometry if SEB (staphylococcal enterotoxin B) can induce Fas-ligand expression on peripheral blood mononuclear cells (PBMC). Second we evaluated cytokine secretion by PBMC with specific ELISAs during SEB treatment and finally investigated if SEB-activated PBMC are able to induce apoptosis in human transitional cell carcinoma cells (TCC) in vitro co-cultures. As proof of concept, we evaluated the toxicity and effects of SEB in a chemically induced transitional cell carcinoma rat bladder cancer model. SEB was administered intravesical once weekly for 6 weeks. Rats with NaCl 0,9% instillation in the same schedule were evaluated as control. Tumor stage, grade and lymphocytic infiltration were assessed on hematoxilin and eosin stained sections. Apoptotic cells in the urothelium and stroma of the bladder were detected by TUNEL. All bladder specimens were stained CD4+/CD8+, ED2 and naphtol AS-D chloroacetate to assess distribution of lymphocytes, macrophages and mononuclear cells.

Results: We demonstrate pronounced time-dependant induction of Fas-ligand on PBMC by SEB. Further, show a massive time-dependant secretion of cytokines IL-2, IFN-gamma and TNF-alpha released from the SEB-stimulated PBMC. In co-culture experiments we demonstrate that SEB-activated PBMC kill TCC cells. TCC cells treated with culture supernatant containing the released cytokines of SEB-treated PBMC demonstrated a minimal response only. In vivo, the toxicity study with up to 100 μg/ml SEB intravesical revealed no side effects of SEB in the animals. For treatment a dose of 10 μg/ml SEB dissolved in NaCl 0,9% vehicle was chosen. Due to narcosis-related deaths, 14/20 animals in the therapy group and 16/20 in the control group were evaluable. Of the SEB treated animals only 3 had a tumor remaining vs. 13 animals with tumor in the control group. In the remaining tumors of the animals in the therapy group, we found a significant amount of apoptosis and a large amount of granulocytes mainly in the urothelium, whereas we found no relevant apoptosis or infiltration of the bladder with lymphocytes and no macrophages in the control group.

Conclusions: The in vitro findings show that SEB induces Fas-ligand expression on immune cells accompanied by a massive release of cytokines kills effectively TCC cells. In vivo, we could validate these anti-tumor observations. Therefore a clinical proof of concept study (first in man) should be initiated.

863 POSTER

Intraoperative and interactive planning for permanent prostate brachytherapy: dosimetric and clinical results

R. Baumann[1], A. Warszawski[1], S. Machtens[2], J.H. Karstens[1]. *[1] Medical University Hannover, Department of Radiotherapy, Hannover, Germany; [2] Medical University Hannover, Department of Urology, Hannover, Germany*

Background: Permanent seed implantation is a well accepted treatment of early stage prostate cancer. Since end of 2000 the interstitial brachytherapy with iodine-125 seeds is performed at the Medical University Hannover with the so called ProSeed-method. Treatment planning is done with the system VariSeed 6.7 and 7.0. With this new version of the planning system