achieved with the combination of GEM and 5-fluorouracil in aRCC pts.; furthermore, our results showed an activity superimposible to that observed with the combination of GEM and Cisplatin. However, the high percentage of patients experiencing long-lasting SD, together with the good toxicity profile we observed, suggests that this regimen deserves further refining and evaluation.

870 POSTER

Long term follow-up in seminoma patients stage I and II A/B after adjuvant irradiation of lymphatic pathways

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Background: Adjuvant irradiation of the lymphatic pathways in seminoma patients is an established treatment. A long-term follow up of more than ten years is rarely reported in literature. The experience of a single institution is presented; recurrences and late effects were evaluated.

Materials and methods: From April 1981 to December 2000 179 patients with a seminoma received irradiation. From 174 patients the records could be evaluated. Median age was 37,8 years (21-74 years) Stage I 156 patients, II A 12 patients and II B 6 patients. In 86 patients the tumour was localized in the right testis, in the left in 84 patients. Histology showed in 167 patients a classical seminoma, in four a spermatocytic seminoma and in the remaining three an anaplastic seminoma. All patients underwent an inguinal orchiectomy followed by irradiation no chemotherapy was administered. Stage I patients received a median dose of 27,7 Gy (1982-1993 26-30 Gy, from 1993 26 Gy n=85), stage II A patients received a median dose of 31,7 Gy and in II B a median dose of 33,5 Gy. Irradiation was delivered with opposing fields using linear accelerator (n=172) and ^{60}Cobalt machine (n=2).

Results: Median follow up for all patients was 89 months. Recurrences occurred in five stage I patients and three stage II patients. One patient developed an isolated in-field recurrence after a dose of 30 Gy. The other locations were mediastinal n=4, inguinal n= 2 and supraclavicular n=1. All patients with recurrences received chemotherapy after biopsy (n=3) or partial surgery (n=3) leading to a complete second remission (median follow up: 66 months, range 5 to 121 months). Recurrence free survival at 10 years was for stage I 95,7% and for stage II 80,8%. Five patients died intercurrent. Overall survival was 91,3% and disease specific survival 100%. No late effects were observed.

Conclusion: The adjuvant irradiation of seminoma patients is well tolerated and able to minimize the risk of a lymph node recurrence. With regard to the benefit the side effects are acceptable.

871 POSTER

Acute toxicity and late GI and GU complications in organ sparing treatment of bladder cancer

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Purpose: To assess the factors predict acute toxicity and late GI and GU morbidity in radiation treatment of the bladder cancer. To investigate whether rectal and bladder volume which are in the treatment field can be used to identify risk groups for developing late gastrointestinal (GI) and genitourinary (GU) complications after organ sparing treatment of Bladder Cancer.

Method and Materials: A total of 41 patients with bladder cancer treated with definitive radiotherapy and with / without concomitant chemotherapy with a minimum of 3 years follow-up were evaluated. Patients were scanned with computerized tomography for treatment planning and treated with conventional box techniques. These patients were treated to a median total RT dose of 66.6 Gy at 1.8 Gy per fraction and 22 patients were treated with cisplatin 30 mg/m2 for 2h IV at weekly intervals in combination with RT. The irradiated rectal surface area for a given dose were calculated for a group of 41 patients treated with a four-field box techniques to a total (tumor minimum) dose range 64.8 to 68.4 Gy. The incidence of acute toxicity and late GI and GU complications was classified using the RTOG/ EORTC and the SOMA/LENT scoring system.

Results: Acute GI (7 patients) and GU (8patients) were noted grade 2 or higher side effects. Two patients had both side effects. GI acute side effects were not correlated with GU acute side effects. Late morbidities were not correlated with acute morbities. Two patients had grade 2 or 3 late effects of GI morbidities. Four patients had grade 2 or 3 late effects of GU morbidities. Higher T stage, involvement of pelvic lymph node and age(> 60 years) were significantly related to late GI and GU morbidity (p=0.061;p=0.014;p=0.001 respectively). The relative rectum wall and filling volumes which are in the treatment field correlated with acute toxicity and late GI complications. Relative bladder filling volumes also correlated with acute toxicity and urinary incontinence.

Conclusions: Both acute toxicity and late GI and GU morbidity demonstrated a volume dependence of rectum and bladder in the treatment field. Moreover both late GI and GU morbidity increased in patients more than 60 years old.

872 POSTER

Rectal toxicity and quality of life after definitive conformal radiation therapy (CRT) of patients with prostate cancer

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Background: To evaluate the impact of chronic rectal toxicity, especially rectal bleeding, on health related quality of life after definitive CRT of localized prostate cancer.

Material and methods: 173 patients were contacted a median of 46 months (24 98 m.) after CRT. Median age was 75 years (57 96 y.). Median dose to the prostate was 70 Gy (59 74 Gy). 80% of the patients had received short term neoadjuvant hormonal therapy before and during RT. Rectal toxicity was evaluated with a standardized 8-item toxicity score and rectal continence was evaluated with the Jorge and Wexner rectal continence score (JW-score). The EORTC quality of life questionnaire C30 (QLQ-C30, version 3) and the prostate cancer module QLQ-PR25 were used to evaluate quality of life. Analysis of variance was carried out to detect associations between rectal toxicity and quality of life.

Results: 25% of the patients stated to suffer presently from rectal bleeding: 10% experienced bleeding less than once/month, 10% had bleeding less than once/week and 5% reported at least weekly bleeding. The prevalence of the other rectal/bowel symptoms was: loss of mucous 10%, defecation pain 8%, bowel cramps 8%, flatulence 42%, diarrhea 26%, urge 27%. Overall 56% of the patients stated some kind of rectal incontinence on the JW-score (JW-score > 0). Rectal bleeding was not associated with global quality of life (QoL) nor with any other of the scales of the QLQ- C30. Patients with rectal bleeding had higher rectal symptom scores on the PR25 bowel scale ($p<0.001$) but rectal bleeding is one of it's items. None of the other rectal symptoms except for incontinence was associated with global quality of life. Patients with a rectal incontinence score of > 2 (n = 51) had worse QoL-values than those with a better or perfect continence (p=0.003). Age or the use of neoadjuvant hormonal therapy did not correlate with global quality of life.

Conclusions: Chronic rectal bleeding after CRT is common but it is mostly intermittent and it does not interfere with the patient's quality of life. Various degrees of rectal incontinence after CRT are frequent. Nevertheless only those patients with a JW-score of > 2 also report lower quality of life scores. Further research is needed to explore if there is an association between rectal continence and dose-volume histogram data.

873 POSTER

Predictors of late rectal and urologic side-effects after conformal radiation therapy (CRT) of patients with prostate cancer

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Background: To evaluate predictors of chronic rectal (GI) and urologic (URO) toxicity after CRT of prostate cancer.

Material and methods: 302 patients with a median follow up of 33 months (12 85 months) were evaluated. Median dose to the prostate was 70 Gy (59 74 Gy). 235 patients (78%) had received short term neoadjuvant hormonal therapy (HT) before and during RT. Toxicity was evaluated with a modified RTOG-score. Every macroscopic rectal bleeding was classified at least as grade II.

Results: Incidence of GI toxicity: table 1; Incidence of URO toxicity: table 2. No grade IV or grade V side-effects were observed.

Correlation of the following variables with grade II/III late toxicity was evaluated: Age, body mass index, prostate dose, inclusion of the seminal

Table 1

GI	stool-frequency	mucous/pain	bleeding
II°	3%	2%	21%
III°	1%	0%	1%

Table 2

URO	pollakisuria	nycturia	pain	hematuria	stenosis
II°	9%	23%	9%	5%	0.3%
III°	3%	3%	2%	1%	2%

vesicles, neoadjuvant HT, diabetes, cardiovascular disease, acute toxicity > I°. Univariate predictors for a higher incidence of late side-effects were: GI: prostate dose (p=0.035) and acute toxicity (p=0.005); URO: body mass index (p=0.059), cardiovascular disease (p=0.036) and acute toxicity (p=0.002). Multivariate predictors were: GI: acute toxicity (p=0.004) and prostate dose (p=0.032), URO: acute toxicity (p=0.002) and cardiovascular disease (p=0.023).

Conclusions: The incidence of moderate (III°) rectal or urologic late toxicity after CRT is low (<5%). The occurrence of acute symptoms > I° is a predictor for late II°/III° toxicity.

874 POSTER

Ir192 conformal brachytherapy and external beam radiation (EBR-CU.ir192) with or whithout hormonotherapy for locally advanced prostate adenocarcinoma: the Centre François Baclesse experience

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Technique: We use temporary transperineal implantation with 2 to 6, 20 cm divergent needles. Implantation is made in 20 mn with general or rachianaesthesia. Needles are loaded with Ir^{192} (low dose rate, LDR) or linked to a projector (high dose rate, HDR).

Treatment protocol: The first protocol involved 15 Gy LDR Cu.Ir^{192} and 45 Gy pelvic EBR. The second protocol combined 2 x 4.7 Gy HDR Cu.Ir^{192} and 45 Gy pelvic EBR. The maximum dose delivered to urethra was 2 x 9 Gy. Within the prescribed radiation doses, the dose rate had no influence on clinical results as well as on toxicity. In locally advanced tumours (T2b-c,T3a-b), hormonotherapy (androcur, nonsteroid antiandrogens or LHRH agonists) was given to 83 patients because of dysuria, postponed therapy or based on recent published findings. Hormonotherapy duration was less than 6 months in 82% of patients.

Study population: From July 1989 to September 1999, 693 patients were treated of whom 291 presented with locally advanced N0, M0 tumours. 208 patients were given EBR-Cu.Ir^{192} only and 83 EBR-Cu.Ir^{192} and hormonotherapy. The two patient groups were similar for age (71 and 70 years in average) and WHO 2-3 performance status (36% and 37%); they differed for Gleason grade (grade ≥ 7: 35% versus 66%, p<0.001) and *ab initio* PSA level (> 20 ng/ml: 52% versus 81%, p=0.002).

Results: The 7-year cause specific survival rates were 85% and 75% in patients treated with and without hormonotherapy, respectively (p=0.59). The 7-year cumulative rates of local failure were 12% and 21% (p=0.10); that of distant metastases were 29% and 28% (p=0.79) and that of biological failure (PSA > 4 ng/ml) were 68% and 63% (p=0.58), respectively. Hormonotherapy duration (< 6 versus ≥ 6 months) had no statistical significant influence on local failure, distant metastases as well as biological failure rates although a trend was observed for less local failure with prolonged hormonotherapy (0% versus 15%). According to the Soma-Lent system, the 7-year cumulative rates of grade II-III urinary and digestive complications were 27% and 7%, respectively, similar in patients given or not hormonotherapy. Sexual complications could not be studied because of the deleterious impact of hormonotherapy on sexual performance.

Conclusion: The contribution of hormonotherapy to EBR-Cu.Ir^{192} is limited in patients with locally advanced prostate adenocarcinoma. Its impact might only concern the incidence of local failure. The administration of hormonotherapy immediately after radiation therapy only is questioned in the light of its efficacy when given at the time a local failure occurs.

875 POSTER

A prospectively randomized phase II trial of pegylated doxorubicin in hormone refractory prostate cancer

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Introduction & objectives: Liposomal encapsulation of doxorubicin (Caelyx™) has been shown to reduce non-specific drug delivery to normal tissues and improve the specific delivery to malignant cells. Caelyx™ may also reduce the peak plasma levels of doxorubicin that may be responsible for toxicity. Since doxorubicin shows response rates of 30% in HRPCA, we conducted a prospective randomized clinical phase II trial to evaluate the feasibility, toxicity and therapeutic efficacy of Caelyx™ in HRPCA.

Patients & methods: 48 patients with progressive HRPCA after hormonal therapy and antiandrogen withdrawal were randomized to receive Caelyx™ at 25mg/m^2 every 2 weeks for 12 cycles (group 1), 50mg/m^2 every 4 weeks for 6 cycles (group 2) and 50mg/m^2 every 4 weeks for 3 cycles followed by 40mg/m^2 every 4 weeks for 3 cycles (group 3). All patients received dexamethason 8mg bid on days 1 through 5 and vitamin B 300mg/day. 38/48 patients (79%) presented with severe pain due to osseous metastases equivalent to a pain score of 7.5 on a VAS ranging from 0 to 10. Therapeutic efficacy was recorded by serial PSA serum measurements, toxicity was recorded according to NCIC/CALBG and EORTC QLQ-C30.

Results: Median age was 68.9 (range 58-79) years; mean follow-up was 42 months. Mean pre-therapeutic PSA was 660.4 (8-6340) ng/ml. An objective response (>50% PSA↓) was observed in 17/25 (68%) patients in group 2 and the mean response duration was 6.5 months. None of the remaining patients developed a PSA response. Significantly more patients in group 2 had a pain response (52.6%) than patients in group 1 and 3 (28.6%, p=0.04). Mean 1-year survival was significantly higher in group 2 (42%) than in groups 1 and 3 (6% and 20%, respectively, p=0.02). Toxicity was severe with 24 pts (50%) demonstrating WHO stage III/IV toxicity. There was a significant difference in the type of toxicity between the different groups. Palmar-plantar erythema developed in 60% of group 1 patients (p<0.0005) whereas tachycardia developed predominantly in groups 2 and 3 (20% and 80%, p<0.0005). There was no dose-limiting cardio- or hematotoxicity.

Conclusions: Pegylated doxorubicin has a high palliative efficacy in HRPCA with painful osseous metastases; a short-term objective response was observed in the 40mg/m^2 group. Caelyx® might be a useful component of chemotherapeutic combination therapy in HRPCA.

876 POSTER

Protein microchips for the analysis of prostate specific antigen

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Background. DNA and protein microchips found wide application in different fields of fundamental and applied science. Three-dimensional gel-based biochips with immobilized proteins developed by the Engelhardt Institute of Molecular Biology RAS can be used for different types of analysis including immunoassays. The goal of our studies was to create microchip-based technique for quantitative assay of prostate cancer marker, prostate-specific antigen (PSA, total and free) in sera of cancer patients.

Material and methods. Microchips with immobilized antibodies to total and free PSA were manufactured. The chip is an array of three dimensional semi-spherical gel elements separated from each other with hydrophobic surface. For the microchip fabrication, solutions of co-polymerization mixtures containing gel monomers and proteins were spotted on a glass slide by a robot. Diameter of gel drops was 50ñ300 μm depending on a robot pin. Polymerization of gel arrays was carried out under irradiation with UV