pelvic (IWP), and low pelvic (LP) fields. We recorded the grade of diarrhea according to the common toxicity criteria (CTC) until 39.6 Gy. The overall and ∗Grade 2 diarrhea rates were compared among groups.

Results: The diarrhea rate was 86%, 78%, and 63% (p=0.0058) in patients with WP, IWP, and LP fields, respectively. The corresponding rate of ∗Grade 2 diarrhea was 27%, 16% and 17% (p=0.0914). The distribution of full dose volume was 18% (NVWT), 62% (SVWT), and 20% (LVWT). The diarrhea rate of WP fields was 63%, 95%, and 92% in the NVWT, SVWT, and LVWT group (p=0.0088), respectively. The corresponding rate of ∗Grade 2 diarrhea was 6%, 22%, and 46% (p=0.0154). For patients with WP irradiation, small bowel within target (S VWT+LVWT) was the factor predictive for risk of overall diarrhea in both univariate (p=0.0021) and multivariate (p=0.0016) analysis. More amount of small bowel within target was the only factor predictive for risk of ∗Grade 2 diarrhea in both univariate and multivariate (p=0.0154) analysis.

Conclusion: Whole pelvis irradiation resulted in higher incidence of overall diarrhea. Overall incidence of diarrhea is always higher while small bowel is within the whole pelvic target. There is a positive correlation of small bowel amount within whole pelvic target and incidence of ∗Grade 2 diarrhea. The scoring method may be used to evaluate risk of diarrhea before whole pelvic irradiation.

502 POSTER

Repopulation of the moderately well differentiated GL human squamous cell carcinoma growing in nude mice

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Purpose: Several clinical trials and experimental investigations showed important influence of overall treatment time on results of fractionated radiotherapy (RT). This so-called time factor has consistently been observed in human squamous cell carcinoma (hSCC) and is considered to be caused by accelerated repopulation of clonogenic tumour cells. It has been suggested that, reminiscent of the regulated proliferative response of normal squamous epithelium, SCC which have preserved characteristics of differentiation have a greater repopulation capacity during fractionated RT than undifferentiated tumours. The aim of the present study was to investigate repopulation in moderately well differntiated GL hSCC in nude mice.

Methods and Material: GL hSCC were transplanted subcutaneously into the right hindleg of nude mice. Tumours were irradiated every, every 2nd or 3rd day with 6, 12 or 18 fractions (fx) of 5.4 Gy (clamp) or 2.0 Gy (ambient), assumed OER = 2.7. Graded top-up doses were applied under clamp hypoxia, to determine the tumour control dose 50% (TCD50).

Results: With increasing number of daily 5.4 Gy fx under clamp hypoxia the top-up TCD50 values decreased significantly from 50.9 Gy [95% CI 47, 54] after single doses to 0 Gy after 18 fx. For the same number of fx the top-up TCD50 increased with increasing overall treatment time. The results are consistent with a constant repopulation rate with a clonogenic doubling time (Tclon) of 12.7 days [8.6, 16.8]. Under ambient blood flow the top-up TCD50s for daily 2 Gy fx decreased significantly but less pronounced than for 5.4 Gy under clamp hypoxia. For a given number of fx under ambient conditions the top-up TCD50s did not increase significantly with overall treatment time except for RT with 12 fx in 36 days compared to 12 and 24 days. The Tclon value from these data was 27.7 days [11.6, 43.8] Conclusion: Our data demonstrate significant capacity for repopulation of clonogenic tumour cells during fractionated RT of GL hSCC under clamp hypoxia without indication of a change of the repopulation rate during treatment. Less pronounced repopulation was observed for RT under ambient conditions, which might be explained by preferential survival of hypoxic and therefore nonproliferating cells. Taken together with our previous studies on poorly differentiated FaDu tumours the results support important heterogeneity of kinetics and mechanisms of repopulation in different experimental SCC.

503 POSTER

Quantification of a differentially expressed gene, RTP801, in irradiated HeLa cells using real time PCR

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Purpose: RTP801, a hypoxia-inducible factor-I-responsive gene, was cloned and characterized in MCF7 human epithelial breast carcinoma cells in 2002 and was strongly up-regulated with hypoxia. We tried to quantify the scarce RTP801 mRNA accurately and to compare the gene expression patterns of irradiated HeLa cells and non-irradiated controls.

Materials and Methods: Cells were harvested and total RNA was extracted 4 h after exposure to 0.1, 0.5, 1, or 2 Gy. We performed real-time PCR using CYBR green I dye with the iCYCLER IQ system from BIO-RAD.

Results: A 200-fold decrease was observed at 0.1 Gy, while the response subsequently declined at 0.5, 1, and 2 Gy, by 11, 6, and 2.5 times, respectively.

Conclusion: We observed that doses in the range 0.1-2.0 Gy reduced the amount of RTP801 mRNA at a given time. Interestingly, the lowest dose, 0.1 Gy, clearly decreased transcripts more than the higher doses. These results demonstrate that it is possible to identify and quantify differential gene expression using sparse mRNA with real time PCR. Further studies of down-regulation in *RTP801* gene expression and the implications of the strong response to low doses could be useful for elucidating the biological response of HeLa cells to radiation and developing novel therapeutic targets.

504 POSTER

Quality aspects and time gain of an automated procedure for generating an optimized plan in the routine treatment of breast cancer with external tangential beam irradiation.

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Background: We use two tangential, single isocentre, photon half beams as standard technique for breast irradation in our center. On average 275 patients are treated yearly for breast cancer using this setup. Every patient has a planning CT in treatment position of at least the treated region (average 15 cm cranio caudally) and the neighbouring tissues with a margin of 4 cm. At 1 cm interval this leads up to a total of about 25 CT slices per patient. The routine and reproducible drawing of the CTV and the skin on all these CT slices takes considerable time. We investigated if this time could be reduced by automating part of this work and automating the planning optimization procedure.

Material and methods: To delineate the breast contour we use a lead collar around the conserved breast or chest wall. A maximum of 3 cm of projected lung tissue is accepted by setting the gantry, collimator angle, field aperture and isocentre. A third beam (called collar beam) uses the same isocentre and is used only for the contouring software. Its gantry angle is orthogonal to the axis of the tangential beams and the aperture includes the complete palpable breast contour delineated by the lead collar. From the combined use of the CT data, the location of the isocenter and this collar beam a fully automated procedure was developed for the delineation of the planning optimization volume and PTV and the computer optimized planning procedure.

Results: In a feasibility study 43 consecutive and unselected patients were included. Three different plans were considered: (1) a 2D plan using only one slice, on screen manual contouring and dosimetrist-guided

Partial volumes of relevant organs at risk for right and left-sided breast tumors with the three planning procedures

	Partial volume in cc					
	Right-sided tumors			Left-sided tumors		
	2D	3D	CMI	2D	3D	CMI
Lung						
Volume receiving more than 20 Gy	132.1	162.7	127.4	120.6	116.4	108.7
Volume receiving more than 40 Gy	71.2	71.6	72.3	64.3	65.9	53.4
Heart						
Volume receiving more than 20 Gy	0.01	0	0	8.2	5.9	6.1
Volume receiving more than 40 Gy	0	0	0	5.4	3.8	4.1

optimization, (2) a 3D plan using all slices with dosimetrist-guided optimization and (3) a computer-optimized plan with automatic contouring and constrained matrix inversion (CMI) optimization. The resulting dose distributions (DVH) on the same organs at risk were compared in order to verify that the automatic procedure did at least as good as the classical manual method. Results for the irradiated partial volumes of relevant organs are listed in the following table.

The total planning procedure took about 25 minutes of which less than 10 minutes were needed for human interaction.

Conclusions: This automatic technique shows acceptable results concerning the partial lung- and heart volume that was irradiated and the procedure reduces the work at the computer planning level at the expense of some more time at the simulator step (third beam).

505 POSTER

High-dose-rate intracavitary brachytherapy alone in post-hysterectomy for endometrial carcinoma

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Purpose: To evaluate local control, toxicity and survival among patients (pts) with endometrial carcinoma stage I and II submitted to post-hysterectomy adjuvant high-dose-rate (HDR) intravaginal brachytherapy (IVBT).

Methods and Materials: Between April 1997 to December 2001, 71 pts with endometrial adenocarcinoma stage I and II who underwent total hysterectomy with bilateral salpingo-ooforectomy including negative lymphadenectomy were submitted to IVBT (HDR), as exclusive adjuvant therapy. The median age of pts was 64 (43-85) years. The surgical staging according (1988 FIGO classification), and histologic grade was the following: pT1b/G1-42 pts, pT1b/G2-18 pts, pT1b/G3-1 pts, pT1c/G2-4 pts, pT1c/G3-2 pts; pT2a/G1-3 pts, pT2b/G3-1 pts. Vaginal BT was given in 4 weekly fraction of 6 Gy, prescribed at 5 mm depth from applicator surface. Toxicity was evaluate according to EORTC/RTOG score

Results: With a median follow time of 34 (12-68) months, 70 pts are alive and one patient died with breast cancer without evidence of endometrial disease. The 5 years overall survival and disease free survival probability was 98,5% and 93,4% respectively. Recurrence were observed in four pts (5,5%) during the first 2 years:1 pt experienced a low vaginal recurrence concomitantly with femoral nodes and was submitted to a external beam radiotherapy (EBRT), 2 pts developed a pelvic mass and were submitted to surgery followed by EBRT, and 1 pt with peritoneal carcinomatosis, after 11, 6, 15, and 14 months respectively. The median follow-up time after recurrence was 7,3(3-36) months.All patients were alive at end of the study. The overall late toxicity was low, and no grade 3 or 4 complication were recorded

Conclusion: Post-operative intravaginal BT in pts with surgical stage I and II endometrial adenocarcinoma, achieve local control, with minimal morbidity.

506 POSTER

Definitive radiotherapy for cervical cancers: Retrospective analysis of 449 patients treated with external beam-radiotherapy (EBRT) and high-dose-rate-afterloading (HDR)with more than 5 years follow-up

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Purpose: Definitve radiotherapy in the treatment of cervical cancers is a treatment option with excellent clinical results. Presented were the results of a retrospective analysis of cervical cancers how were treated in our department of radiotherapy.

Material & methods: Between 1987 -1995; 449 pts. with cervical cancers were treated with a combined treatment schedule with curative intention. The treatment included in all cases external beam radiation (EBRT) and high-dose-rate afterloading with Iridium-192 (HDR-Al). Chemotherapy was not administered. The mean age of all patients was 53 years (27-85 years).The EBRT included in 440 patients only the pelvis, in 9 cases also the paraortal lymph nodes. The single dose ranged from 1.8-2.0 Gy, the total dose from 38 Gy up to 60 Gy in point B. The HDR-Al ranged in 97% of the cases in 7-8 Gy single dose and 4 to 5 fractions. The total dose in point A was 68-75Gy (in 82% of pts.) and 50-56Gy in point B (96% of pts.).

Results: The 5-year-results dependent on tumor stage (FIGO) were: Stage IA and IB (N=87) 87 ± 4%; stage IIA and IIB (N = 155) 79 ± 4%; stage IIIA and IIIB (N = 194) 53 ±4%; stage IVA (N = 13) 37 ± 18%. Anemia had also an impact on survival (11g/dL; p

507 POSTER

Impact of anemia on tumor oxygenation and clinical outcome in cervical cancers treated with definitive radiotherapy

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Background: Hypoxia in general is a complex phenomenon. The presence of hypoxia in malignancies is associated with a decrease of prognosis. Anemia in patients with cervical cancers is also an independent predictor in poor outcome. In our investigation we have determined anemia and tumor oxygenation as prognostic factors in advanced cervical cancers who were treated with radiotherapy with regard to correlation of anemia and tumor hypoxia.

Material and Methods: 87 patients with locally advanced squamous cell cervical carcinoma FIGO IIB-IVA were investigated from March 1995 to Dec. 2000. All were treated with definitive radiotherapy with curative intent by a combination of external radiotherapy plus HDR-afterloading. The tumor oxygenation was measured using the Eppendorf-device prior to the radiotherapy and after 19,8Gy.

Results: The 3-year-survival was in stage IIB 72% (N=19); IIIB (N=59) 60%; IVA (N=9) 22% (total 57%). Our investigation showed a significant impact of change of tumor oxygenation during radiotherapy on survival: Cancers with high median pO2 prior or during radiotherapy had a 3-year-survival of 68% in comparison to cancers with persisting hypoxia (38%). The survival of anemic patients (hb < 11g/dl) was significantly lower (31%) than of non-anemic patients (64%), p = 0,04. A correlation between hemoglobin-level and tumor-hypoxia during radiotherapy after 11 fractions was observed (p <0,01). In a multivariate analysis only tumor stage (p =0,003) and hemoglobin-level during radiotherapy showed a significant impact on overall survival (p = 0,005) and local response (p = 0,0001). The tumor-pO2 measured after 19,8 Gy had a correlation to local control (p = 0,042). The pO2, measured prior to radiotherapy, was without importance on clinical outcome.

Conclusions: Advanced stage and hemoglobin level during radiotherapy are independent prognostic factors in cervical carcinomas. In summary, the association between hemoglobin and hypoxia during radiotherapy suggest the importance of hemoglobin substitution in anemic cancer patients during radiotherapy.

508 POSTER

Hemoglobin levels during radiation therapy and their prognostic influence on local control and survival of patients with endometrial carcinoma

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Background: Anemia is a common complication of cancer that has been associated with poor response to treatment and decreased survival in a number of malignancies.

Material and Methods: A retrospective chart review was undertaken to determine the effects of hemoglobin levels, measured prior to and during radiation therapy, clinical prognostic factors (e.g. age, body mass index, tumor stage) in altogether 996 endometrial cancer patients treated between 1986 and 1998. Most of them received adjuvant radiotherapy (724/996; 72.7%) but also many underwent primary radiotherapy, in particular because of concomitant diseases, e.g. which did not allow general anesthesia (185/996; 18.6%). None of the patients received recombinant human erythropoietin. Classification of anemia followed WHO recommendations (anemia < 11 g/dL). The difference between observed overall survival and its predicted value was computed by multiple regression analysis for each patient with respect to prognostic factors.

Results: Preoperative hemoglobin levels were of no prognostic value. Normal hemoglobin levels prior to treatment showed a trend towards improved survival in patients undergoing primary radiotherapy (p < 0.1). Anemia, however, was significantly associated with poor survival in patients undergoing adjuvant radiotherapy (p < 0.001). The course of hemoglobin during adjuvant radiotherapy played an important role. Survival was improved in patients without anemia compared to patients who developed anemia, who were anemic during radiotherapy, or those whose hemoglobin