rence, and complication rate of rectum and bladder between HDR and LDR ICR in each study. Homogeneity tests were conducted before the integration of each effect size into a common effect size. The common effect sizes and 95% confidence intervals (CI) were calculated using either the fixed or the random effect model according to the results of the homogeneity tests.

Results: We performed meta-analysis with the data of 18,629 patients including 10,689 patients receiving HDR ICR and 7,940 patients receiving LDR ICR in 14 selected articles. The common effect sizes for 5-year survival rate, 5-year disease free survival rate and local recurrence rate were 1.1869 (95% CI: 0.9875-1.4264), 1.2037 (95% CI: 0.6284-2.3059), and 0.8926 (95% CI: 0.7330-1.0869). The common effect sizes for moderate to severe complication rates of rectum and bladder were 0.8625 (95% CI: 0.5877-1.2657) and 1.0937 (95% CI: 0.778-1.5375). There were no significant differences in 5-year overall survival, 5-year disease free survival, local recurrence and complication rates of rectum and bladder between HDR ICR and LDR ICR.

Conclusions: This study suggests that conventional LDR ICR could be replaced by HDR ICR which is safer and more convenient for patients and medical personnel. To determine the proper fractionation scheme for HDR ICR, additional well-designed prospective studies should be followed.

499 POSTER

CT-based three-dimensional intracavitary brachytherapy planning in cervix cancer: Is it always better than conventional planning?

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Background: Intracavitary brachytherapy in cervix cancer is usually based on conventional orthogonal radiography-based planning (CP) notwithstanding the advances of imaging and three-dimensional planning technique (3DP). The purpose of this study is to compare CP with CT-based 3DP and to find the problems adapting 3DP into routine practice.

Materials and Methods: Thirty cervical cancer patients receiving Ir-192 HDR brachytherapy after external 30-40Gy RT were investigated. All patients underwent CT scanning and 3DP with CT images. For the CP, CT images, not orthogonal radiography, were used by digitizing point A, rectum, bladder points on CT to keep the same patient 's position and applicator geometry of two planning methods. Fractional 100% dose was prescribed to point A in CP and PTV (GTV+safety margin) in 3DP. Rectal-bladder ICRU and maximum point doses, volumes receiving 100% dose, surplus volumes (100% volume minus PTV) and rectal, bladder DVH were analyzed. The planning system PLATO was used.

Results: The mean pre-RT tumor size by MRI was 4.1cm. The mean volumes of GTV, PTV, rectum and bladder were 15.6, 31.5, 72.3 and 127.4cm^3, respectively. Patients were divided into Group A and B by which 100% isodose line prescribed to point A fully encompasses PTV or not. The number of Group A patients whose PTVs are fully surrounded by 100% line was 20 and Group B was 10. The mean GTV (11.6 cm^3) and PTV (24.9 cm^3) of Group A were smaller than those (23.7, 44.7 cm^3) of Group B ($p=0.003$). For the CP, the results of point doses and volumes showed no difference between two groups. For the 3DP, Group B suffered from large normal tissue doses and volumes significantly ($p<0.05$). In comparison between CP and 3DP in all 30 patients, though the mean 100% dose volume and surplus volume of 3DP were smaller ($p=0.003$ and 0.004), the results of organs at risk showed no difference except dose % irradiating to 50% volume of bladder (CP 36.4% vs 3DP 27.2%, $p=0.03$). In Group A, 3DP showed significant superior results to CP including organs at risk doses and volumes ($p<0.05$). However, in Group B with large tumors, the mean rectal and bladder irradiating doses and volumes were much higher in 3DP ($p<0.05$).

Conclusions: Although CP with point A prescription generally overestimates PTV, CT-based 3DP gives too much irradiation to organs at risk in large tumors. Other technique including interstitial implant or dose supplement to PTV without organs at risk should be considered in these cases.

500 POSTER

Dosimetric study of boron neutron capture therapy (BNCT) for multiple liver tumors: dose-volume histogram analyses using the simulation environment for radiotherapy applications (SERA) treatment planning system

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Background: Using a rat liver tumor model, we have successfully selectively accumulated high 10-boron concentrations in experimental liver tumors by intra-arterial administration of borocaptate sodium (BSH)/lipiodol emulsion. The present study aimed to investigate the feasibility of treating multiple liver tumors with boron neutron capture therapy using BSH/lipiodol emulsion (BSH/lipiodol-BNCT), from the viewpoint of dosimetry using the Simulation Environment for Radiotherapy Applications (SERA) system; a currently available BNCT treatment planning system.

Material and methods: Computed tomography images of four patients with multiple liver tumors were incorporated into the SERA system. Three treatment plans for irradiating the whole liver with BSH/lipiodol-BNCT using two or three epithermal neutron beams in one fraction were generated for each patient. The beam directions were as follows; anterior-posterior (AP), anterior-right (AR), and anterior-right-posterior (ARP). The 10-boron concentrations in the tumor and the liver applied in the present study were 197.3 and 15.3 ppm, respectively; the levels were obtained from experimental studies in animals. For comparison among the treatment plans, all plans were normalized to deliver a mean dose of 5 gray-equivalent (Gy-Eq) to the whole liver. The mean doses and the therapeutic gain factors for the tumors, defined as minimum dose to the tumor / maximum dose to the liver, and the inhomogeneity index of the thermal neutron fluence for the whole liver, defined as maximum fluence - minimum fluence / mean fluence were evaluated in each plan.

Results: Dose volume histogram analyses were applied separately to tumors in the left and right lobes. The mean dose delivered to the tumors in the right lobe by ARP-beams was significantly higher than that by AP-beams (65.1 $\pm$ 19.5 vs. 45.6 $\pm$ 19.1 Gy-Eq). The therapeutic gain factor for the tumors in the right lobe by ARP-beams was significantly greater than those by AP- or AR-beams (6.1 $\pm$ 2.1 vs. 3.8 $\pm$ 1.8; and 6.1 $\pm$ 2.1 vs. 4.5 $\pm$ 2.1). The mean dose delivered to the tumors in the left lobe by AP-beam was 53.3 $\pm$ 23.4 Gy-Eq, which was higher than 45.1 $\pm$ 19.4 Gy-Eq by AR-beams or 39.9 $\pm$ 15.5 Gy-Eq by ARP-beams, but not significantly. The therapeutic gain factors for the tumors in the left lobe were 3.8 $\pm$ 2.4 (AP), 3.5 $\pm$ 2.2 (AR) and 3.5 $\pm$ 1.8 (ARP), respectively. The inhomogeneity index of the thermal neutron fluence for whole liver using ARP-beams was lower than those by AP- or AR-beams.

Conclusions: ARP-beams can deliver the most homogeneous distribution of thermal neutron fluence to the whole liver, and provide the greatest therapeutic gain factors for tumors in the right lobe, along with approximately equal therapeutic gain factors for tumors in the left lobe, compared with the AP- or AR- beams. From a dosimetric viewpoint, the BSH/lipiodol-BNCT treatment plan using three epithermal neutron beams is the most suitable for treatment of multiple liver tumors.

501 POSTER

Effects of topographic distribution of small bowel and field sizes on acute diarrhea in gynecologic patients undergoing pelvis irradiation

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Background: To find the topographic distribution of the small bowel within target and correlate both target volume and small bowel amount of full dose and risk of diarrhea during pelvic irradiation in patients with gynecologic malignancies.

Materials and Methods: We reviewed 295 patients with cervical or uterine cancer managed by 4-field pelvic irradiation from January 2000 through January 2003. According to contrast within small bowel in simulation films, we categorized small bowel volume of full dose as no volume within target (NVWT) , small volume within target (SVWT) , and large volume within target (LVWT) group. External pelvic irradiation (39.6-45 Gy/ 22-25 fractions) was delivered to all patients initially. For investigating effect of field size, we categorized fields as whole pelvic (WP), inadequate whole

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