subjects (Mann Whitney U, p<0,05), no change was determined after irradiation. Comparing to control levels, no significant difference was found in GSH levels of cancer patients. They were observed to be decreased by abdominal irradiation (Wilcoxon signed rank test, p<0,05). All the plasma levels were found to be unaltered by head &neck irradiation. There were no significant correlations between the plasma levels of the parameters and sex. A correlation was observed between the plasma MDA levels and age (Pearson 0.578, p<0,05).

Conclusion: Except for the well-known radiation-induced damage, radiation effect is characterized by different biochemical derailments on different anatomic localizations and RT techniques. The alterations of the parameters indicate enhanced oxidant stress and different antioxidant requirements after RT. This observation provides further evidence for the need of detailed biochemical monitoring during irradiation.

527 POSTER

Movement of calcified mediastinal lymph nodes with breathing

P. Jenkins, C. Salmon, C. Mannion. *Gloucestershire Oncology Centre, Cheltenham General Hospital, Cheltenham, United Kingdom*

Introduction: Lung tumour motion with breathing can result in inadequate coverage of disease by radiation treatment portals. To compensate for movement large safety margins are added around the CTV. However this strategy increases the risk of normal tissue toxicity and limits the scope for dose escalation. Previous studies have reported significant displacements of primary intrathoracic tumours with breathing (>10mm). However the movement of mediastinal lymph nodes has not been defined. We noted that occasional patients referred for thoracic irradiation had calcified mediastinal lymph nodes (LN) identifiable on fluoroscopy. We propose that these 'visible' LN represent practical surrogate by which to estimate the general breathing motion of LN involved with tumour.

Methods: Patients with primary lung tumours were selected for this study on the basis of the presence of calcified LN visible on fluoroscopy. 24 calcified LN were identified in 15 patients (14 NSCLC, 1 SCLC). Spirometric testing showed that 8 had restrictive defects compatible with chronic obstructive pulmonary disease and emphysema. Nodes in the following ATS stations were identified: 2R(1), 4R(7), 7(2), 8(1), 10R(3), 11R(8), 11L(2). LN mobility during quiet breathing was monitored by fluoroscopic screening performed with arms abducted. Images were recorded at the extremes of respiratory excursion using gantry angles of 0 and 90.

Results: The mean movement (mm) of LN in the cranio-caudal (c.c.) direction was 5.1 (C.I. 3.6-6.7). In the dorso-ventral (d.v.) and medio-lateral (m.l.) directions the observed displacements were 2.1 (C.I. 1.1-3.2) and 1.6 (C.I. 0.8-2.4) respectively. There was a correlation between movement in the c.c. and d.v. or m.l. direction (r = 0.55 and 0.55; p≈ 0.005 and 0.011 respectively). There were no significant differences seen between the movement (expressed as a cartesian vector) of mediastinal (5.5) vs intrapulmonary (6.4) nodes or supra (6.6) vs infra (5.7) carinal nodes. There was no correlation between spirometric parameters or tumour size/stage and movement.

Conclusions: We have demonstrated that the movement of calcified LN during breathing can monitored by fluoroscopy in a cohort of patients with lung tumours. The displacements of these LN during quiet breathing is anisotropic and smaller than that previously reported for primary lung tumours. These data should be incorporated into the expansion algorithms used to define the PTV.

528 POSTER

The choice of optimal radiotherapy technique for locally advanced maxillary carcinoma using 3D treatment planning system

D. Mileusnic, B. Pantic. [1] *Military Medical Academy, Department of Radiotherapy, Belgrade, Yugoslavia*

Purpose: To compare the isodose distribution of three radiotherapy techniques for locally advanced maxillary synus carcinoma and analyze the potential of 3D conformal radiotherapy planning to achieve adequate target dose delivery and sparing of uninvolved healthy tissue structures. **Patients and Methods:** CT scans of forteen patients with T3-T4,N0,M0 maxillary synus carcinoma were acquired and transferred to treatment planning system. A conventional 2D treatment plans with classicaly shaped one anterior + two lateral opposite fields and two types of 3D conformal radiotherapy plans were compared for each patient (*3D-S plan:* MLC shaped one anterior + two lateral opposite fields; *3D-NS plan:* MLC shaped three noncoplanar fields). The target volume and uninvolved dose limiting structures were contured on axial CT slices throughout the volume of interest. The planning parameters for these volumes and degree of neurooptic structures and parotid glands protection were evaluated for all three techniques. A comparison of plans and treatment techniques was assesed using isodose distribution, dose statistic and dose volume histograms.

Results: The best conformity of dose delivered to target volume was achieved with 3D-NS technique and significant differences were found comparing 3D-NS vs. 2D (D*max*: p<0,05; D*aver*: p<0,01; D*min*: p<0,05; V90: p<0,05 and V95: p<0,01) and 3D-NS vs. 3D-S technique (D*min*: p<0,05; V90: p<0,05 and V95: p<0,01) while there were no differences for 2D vs. 3D-S technique.The 3D-S conformal plans were significantly superior to the 2D plans regarding the protection of parotid glands and additional improvement of dose conformity was achieved with 3D-NS technique. 3D-NS technique resulted in decrease of D*max* for ipsilateral retina comparing with 3D-S technique, while (because of beams direction) the level of D*max* for optic nerve was increased (but in acceptable range) with 3D-NS technique.

Conclusion: 3D planning of radiotherapy for localy advanced maxillary synus carcinoma with noncoplanar fields whose number don't exceed the number of fields for conventional arrangement enables the conformal delivering of adequate dose to target volume with improved sparing of contigious uninvolved healthy tissue structures.

529 POSTER

Differential radioenhancing properties of oxaliplatin and cisplatin in human cervical and lung cancer cell lines

E. Weiss[1], M. Rave-Fränk[1], C. Boll[1], O. Pradier[1], J. Lehmann[2], H. Schmidberger[1], C.F. Hess[1]. [1] *University Goettingen, Radiotherapy and Radiation Oncology, Goettingen, Germany;* [2] *University of California, Lawrence Livermore National Laboratory, Livermore, USA*

Objective: Combined modality treatment, including radiotherapy and cisplatin, is now frequently and sucessfully used in the treatment of cervical and lung cancer. Cisplatin has become a standard part of many treatment regimes, but it is not clear whether it is possible to achieve even better efficacy with some other drugs or drug combinations. We tested the combined effects of oxaliplatin and radiation versus cisplatin and radiation using human cervical- and lung cancer cell lines.

Material and Methods: CaSki cervical cancer cells, and A549 lung cancer cells were cultured under standard conditions. Cells were treated with escalating doses of gamma-irradiation (0 - 6 Gy), different doses of oxali- and cisplatin (1 to 20 microM) for 2 hours or 24 hours, or a combination of both. Cell survival was measured by a standard colony-forming assay, after 10 days of growth colonies containing more than 50 cells were scored as survivors. Survival curves, each referring to its specific control were fitted to the data using the linear quadratic model. Sensitizer enhancement ratios (SERs) were calculated at the 37% survival level, and isobologram analysis was applied to test for the drug-radiation interactions.

Results: Oxaliplatin as well as cisplatin alone were cytotoxic in a time and concentration dependent manner, where CaSki cells were more sensitive to drug treatment than A549 cells. After a 2-hour treatment cisplatin was slightly more toxic than oxaliplatin, after a 24-hour treatment both drugs showed the same toxicity. In CaSki cells, oxaliplatin and cisplatin significantly increased radiation toxicity with SERs up to 2.25 for 2.5 mM oxaliplatin given for 24 hours. In A549 cells no increase of radiation toxicity was observed after treatment with cisplatin, however oxaliplatin induced a significant radiosensitization with a SER of 2.30 when 2.5 mM oxaliplatin were given for 24 hours. Isobologram analysis revealed supraadditive interaction between oxaliplatin and radiation in A549 lung cancer cells.

Conclusion: Oxaliplatin had the same effectiveness on tumor cells as cisplatin and induced enhanced radiation toxicity in lung cancer cells, where cisplatin was not effective. This higher potential in combined modality treatment is rendering oxaliplatin to be a promising compound for the modification of radiation response in tumor therapy.

530 POSTER

Evaluation of quality assurance procedure in brain tumors radiotherapy in children

K. Ficek[1], S. Blamek[1], L. Miszczyk[1], K. Slosarek[2]. [1] *Center, Radiotherapy Department, Gliwice, Poland;* [2] *Center, Radiotherapy of planning treatment, Gliwice, Poland*

Purpose: Radiation therapy is effective in brain tumors in children in conjunction with surgery and chemotherapy. Precision volume irradiation

techniques, including three-dimensional conformal irradiation may offer advantage in minimizing irradiated volume and sparing surrounding healthy tissues and protect critical structures. Quality assurance procedures during therapy include: -dosimetry in vivo -positioning accuracy revealed by simulation films and portal images registration Material and Methods: Between 1999 and 2002 42 children with brain tumors were treated in our department with conformal radiotherapy. They were irradiated in supine position with immobilization by orfit masks. During radiotherapy there were 68 dosimetries in vivo of beam axis performed. The portal images were taken at the beginning of treatment and were compared with simulation film. X, Y and Z deviation vectors were calculated. When the action level was unacceptable the patient was repositioned and the procedure started again.

Results: The result showed mean deviation of the ratio of measured to calculated dose at the reference point of 1.4%(-1.9 to 4,2%) SD= ±1.76%. From an analysis of portal films a deviation of the position was 2 mm to 5 mm.

Conclusions: The quality assurance procedures during radiotherapy offers possibility of precise and reproducible treatment. Our system is suitable for routine verification dose delivered to patients and monitoring patients treatment position.

531 POSTER

Radiosentiviity enhancement by a histone deacetylase inhibitor (HDACI), trichostatin A in human glioblastoma cell lines

I.H. Kim[1,2], J.H. Kim[1,2], J.H. Shin[2]. *[1] Seoul National University Hospital, Therapeutic Radiology, Seoul, Republic of Korea; [2] Seoul National University, Cancer Research Institute, Seoul, Republic of Korea*

Background: Histone deacetylase inhibitors (HDACI), novel cytotoxic agents, show *in vitro* and *in vivo* anti-tumor activity for many types of cancer cells and are under clinical trials. But studies addressing the combination with radiation are rare. The purpose of this study is to assess the effect of trichostatin A (TSA), a HDACI, on the radiosensitivity of human glioblastoma cells.

Material and methods: Exponentially growing asynchronous U373MG and U87MG cells were exposed to TSA for up to 24 hrs before irradiation with 4 MV X-ray, and survival was measured by clonogenic assay. The effect of TSA on the cell cycle and apoptosis induction was analyzed by the flow cytometry.

Results: Prior treatment of TSA increased sensitivity of U373MG and U87MG cells at 2 Gy. This effect of TSA was concentration-dependent, but 200 nM TSA was associated with significant direct cytotoxicity as well as radiosensitization with sensitization enhancement ratio of 1.4 to 1.5. Flow cytometry of asynchronous cells exposed to TSA showed the arrest of cell cycle at the G2/M phases and the G1/S transit. Moreover TSA induced apoptosis of glioblastoma cells in a concentration- and time-dependent manner.

Conclusions: This study firstly demonstrated that TSA enhanced radiosensitivity of human glioblastoma cells at as low concentrations as not to cause direct cytotoxicity. Further study addressing the combination of other HDACIs and radiation is going on.

532 POSTER

Analysis of dose-volume parameters for reporting dose distribution in the target volume

A. Terahara, M. Tsubuku, M. Shimada, S. Hayashi. *Toho University Omori Hospital, Radiology, Tokyo, Japan*

Background: Although the dose at the International Committee of Radiation Units and Measurements (ICRU) reference point, the maximum dose and the minimum dose to the target volume are recommended to be reported as a basic requirement, these parameters may not represent inhomogeneous dose distribution in the target volume. We analyzed them together with other dose-volume parameters.

Material and methods: We prescribed radiation doses based on dose-volume histogram (DVH) evaluation and made every effort to minimize the target volume which received less than 95% and greater than 105% of the prescribed dose. In many cases, the mean dose in the target volume was selected for dose normalization and it was occasionally different from ICRU reference point dose. We analyzed the relationship between the reference point dose and dose distribution using DVH in 62 patients with various tumors treated in our hospital.

Results: The doses at the ICRU reference point were smaller than the prescribed doses with a mean of 1.6% and by 3% or more in 13 of 62 cases because we decreased them to avoid hot spots. The mean doses in the target volume corresponded well to the prescribed dose, the difference between them was less than 2% except for one case. The difference between the median dose in the target volume and the prescribed dose was very small and less than 1.2% in all cases. The difference between the maximum dose and the minimum dose ranged from 4 to 77.7% of the prescribed dose with a mean of 24.3%. This difference correlated closely with the difference between the minimum dose and the prescribed dose. This result means that the range of dose inhomogeneity within the target volume reflect cold spot in the target volume. The equivalent uniform dose (EUD) was also calculated, and it seemed reasonable one dose parameter representing both dose level and inhomogeneity. We compared it with ICRU reference point dose, then the difference between them was more than 3% of EUD in 15 cases with a mean of 3.1%.

Conclusions: The ICRU point doses were substantially different from the prescribed doses and EUDs in some patients actually treated in our hospital with our treatment planning method. The maximum and minimum dose could reflect small hot or cold spot which may not have any clinical value. EUD would be a good dose-volume parameter although it should be evaluated with clinical data.

533 POSTER

Hyaluronic acid bladder instillations in the prevention of radiation-induced cystitis

J.M. Delgado, P. Samper, J. Saez Garrido. *Hospital Militar Central de la Defensa, Servicio de Oncologia, Madrid, Spain*

Backgound: Radiation-induced cystitis (RIC), a complication of pelvic cancer irradiation therapy, disrupts the radiation treatment schedule and may hinder the continuation of the therapy completely. The objective of this study was to assess the efficacy of hyaluronic acid (HA, Cystistat®) bladder instillations in the prevention of RIC.

Material and Methods: 90 patients with uterine or cervical cancer (FIGO 3) were reviewed. The patients were divided into 2 consecutive sub-groups of 45 patients, recruited in 2001-2002, and treated within a single center. The 1st sub-group was treated with a standard ambulatory radiation protocol (external radiotherapy: 46-50Gy, brachytherapy: 20-22Gy). The second sub-group received the same radiotherapy plus preventative HA bladder instillations. The instillations of 40 mg/50 mL solution were given during the weekly brachytherapy through the urethral catheter used for the opacification of the bladder. The HA was kept during the dose calculation time for 30-35 min. Evaluations were performed at baseline, 48 hours following each brachytherapy session as well as monthly for three months.

Results: The weekly instillations of HA decreased the risk of infection. Four patients in the first sub-group receiving standard of care had an episode of bacterial cystitis versus none in the second sub-group receiving standard of care and HA bladder instillations ($p<0.002$). There was a decrease in toxicity due to radiation within the sub-group treated with HA. The toxicity (RTOG/EORTC Radiation Toxicity Score) was on average 1.33 in the 1st sub-group versus 0.71 in the sub-group receiving the HA instillations ($p<0.005$) at week 4. At the completion of radiotherapy, the toxicity was 1.24 in the 1st sub-group versus 0.71 in the sub-group receiving HA ($p<0.004$). Two patients of the 1st sub-group reached the grade 3 toxicity versus none in the HA sub-group ($p<0.04$). At the 2 month point of follow-up, nine patients of the 1st sub-group were still experiencing grade 1 toxicity versus none in the sub-group of HA recipients ($p<0.04$). The weekly instillations of HA also positively affected the completion of the treatment within the scheduled time period. The radiotherapy schedule needed to be delayed for two patients in the first sub-group receiving standard of care versus none in the sub-group receiving the HA instillations ($p<0.04$).

Conclusion This retrospective study demonstrates that weekly instillations of HA (Cystistat®) protected the bladder from radiation induced damages and might enhance the comfort and quality of life in these patients. The protective effect in this indication will be the subject of prospective studies.

534 POSTER

Analysis of dose volume histograms in proton therapy for prostate cancer.

K. Nihei, T. Nishio, S. Ishikura, M. Kawashima, T. Ogino. *National Cancer Center Hospital East, Division of Radiation Oncology, Kashiwa, Japan*

Backgrounds: Proton beam, with its physical characteristics, can make it possible to deliver high dose to the target volume without increasing the influence on the surrounding normal tissues. The aim of this study is to