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

evaluate the dose volume histograms (DVH) of rectum and bladder in high dose proton therapy for prostate cancer.

Material and methods: Thirty patients with localized prostate cancer treated by combination of photon/proton therapy (Tx1) were included in this study. *Tx1* consisted of 50 Gy/25 fx photon beam to the prostate and bilateral seminal vesicles (P/SV) by conformal technique of 240 degree-arc followed by proton boost of 26 GyE/13 fx to the prostate (P). For the same patients, we made three different plans of proton therapy as follows; *Tx2*: 50 GyE/25 fx to P/SV followed by 26 GyE/13 fx boost to P, *Tx3*: 76 GyE/38 fx to P/SV, *Tx4*: 76 GyE/38 fx to P. All proton beams were planned in lateral opposed fields. The rectum including filling was contoured from sigmoid flexure to anal verge. The DVHs of rectum and bladder were respectively compared between 4 treatment plans.

Results: V40 (%volume that receives $\geq$ 40 Gy) - V75 of rectum and bladder in 4 treatment plans are shown in Table 1. Percent volumes of three proton plans (Tx2-4) were lower than those of the photon/proton plan (Tx1) in both rectum and bladder, over all dose levels. The DVHs of the plan to deliver full dose to P/SV (Tx3) were similar to those of the other proton plans.

Table 1. % Volume

		V40	V45	V50	V55	V60	V65	V70	V75
Rectum	Tx1	68.3	63.8	60.4	55.1	48.9	43.7	19.4	2.3
	Tx2	33.6	29.5	26.8	22.4	17.7	14.2	8.4	3.5
	Tx3	35.6	31.0	28.3	23.5	18.5	14.6	8.5	3.4
	Tx4	29.9	26.6	23.9	20.2	16.2	13.3	8.1	3.5
Bladder	Tx1	80.4	76.5	73.9	69.9	65.4	62.1	56.5	46.3
	Tx2	56.1	52.8	50.6	47.2	42.6	38.8	32.6	23.6
	Tx3	55.8	52.7	50.4	46.8	42.2	38.8	32.3	23.7
	Tx4	56.8	53.1	51.1	48.0	43.2	38.9	33.1	23.3

Conclusions: Percent volumes of rectum and bladder were reduced in the proton treatment plans, compared with the photon/proton plan. It is suggested that dose escalation for prostate cancer is feasible by proton therapy.

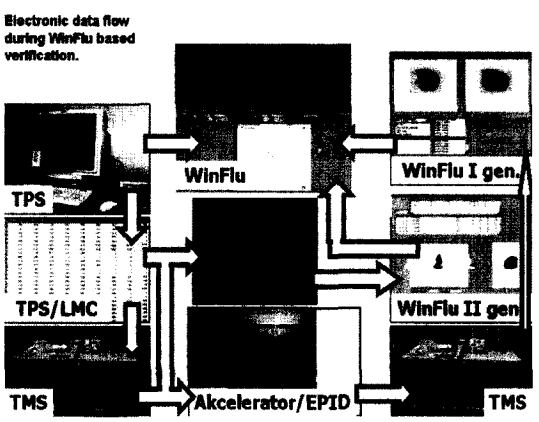
535 POSTER

Verification of Fluence Map (FM) in dynamic radiotherapy techniques

R. Rutkowski, A. Grzadziel, K. Slosarek. *Center of Oncology - Institute, Treatment Planing Unit, Gliwice, Poland*

Background: Comparing to conformal radiotherapy, the Quality Assurance (QA) program for dynamic techniques (Intensity Modulated Radiation Therapy IMRT, Intensity Modulated Radiation Surgery - IMRS) requires some additional procedures. The purpose of the paper is to develop the method for FM assessment obtained from planning, data management and treatment. Presented method is based on WinFlu software originally developed in Treatment Planning Unit in Center of Oncology Institute in Gliwice, Poland.

Material and methods: First FM is imported from Leaf Motion Calculator (LMC) in TPS (CadPlan or BrainSCAN). Second one is obtained from TMS. The WinFlu generates FM to get digital image from static MLC segment positions there. Several images are imported from EPID, then blended by WinFlu generator to obtain third FM. Subsequently images are modified using the gray scale gradient and resolution for comparable conditions. The WinFlu verify three obtained FM by their profiles and gray scale intensity to find out differences. Results are stored to database for future checks and documentation.



Results: The verification method of Fluence Map enables to check dynamic MLC or mMLC plans for any inaccuracy among planning, data management and treatment (LMC/TPS, TMS, EPID).

Conclusions: Verification of the FM based on WinFlu software might constitute a useful method in QA improvement.

536 POSTER

A four dimensional simulation model of the response of solid tumours to radiotherapy in vivo: advances and validation.

V. Antipas[1], G. Stamatakos[1], N. Uzunoglu[1], M. Synodinou[2]. [1] *National Technical University of Athens, Department of Electrical and Computer Engineering, Athens, Greece;* [2] *Metaxa Cancer Hospital, 1st Radiation Therapy Clinic, Piraeus, Greece*

Current radiotherapy (RT) treatment planning (TP) is based on physical optimisation of the dose distribution and on rather crude biological models of tumour and normal tissue response. The introduction of advanced biosimulation methods is expected to substantially improve the RT efficiency. To this end a 4-D patient specific simulation model of the response of malignant tumours to RT schemes *in vivo* has been developed [1,2]. Substantial improvements are presented in this paper.

The Model The imaging data of the patient (e.g. MRI, PET), as well as his/her histopathologic, genetic (e.g. p53 status) and historical data are appropriately collected and introduced into the simulation software. The 4-D simulation procedure is based on the cell cycle, the oxygen and nutrient supply, the LQ model of cell response to RT and the mechanical properties of tissues. The model predictions are visualized using virtual reality techniques (Fig. 1).

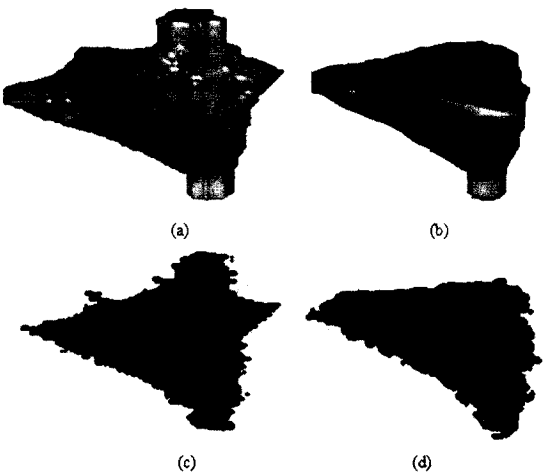


Fig 1. A 3-D visualisation of a glioblastoma multiforme tumour *in vivo*. (a) and (b): external boundary and internal structure of the tumour before RT (c) and (d): 20 days after the beginning of RT (standard fractionation scheme: 2 Gy/day, 5 d/wk, 60 Gy total). Color code: grey: "prolif. layer", dark grey: "dormant layer", black: necrotic layer. A special colouring criterion has been applied.

Improvements A new algorithm leading to conformal shrinkage of the tumour as a response to RT has been developed. Different values for the LQ parameters for each cell cycle phase and the G phase can be introduced based on the experimentally estimated oxygen enhancement ratio. Extensive use of random number generators has been made in order to better simulate the distribution of tumour cells within each given cell cycle phase. Finally, an alternative algorithm accounting for an approximately constant vascularisation field has been developed.

Results The model has been applied to the glioblastoma multiforme case. Various fractionation schemes have been simulated and qualitative agreement with clinical experience has been ensured. A preliminary clinical adaptation and testing process is in progress in the Metaxa Cancer Hospital. Large scale clinical tests have been planned to take place after completion of the preliminary testing stage.

Conclusion Qualitative agreement of the improved model with the clinical experience is followed by clinical tests. The final software is to be used as a decision support and biological TP system by performing *in silico* experiments.

References

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