

and 46% respectively. Squamous cell carcinoma was associated with a better outcome than adenocarcinoma ( $p=0.0189$ ). Chemotherapy was not found to be a significant factor predicting for local control ( $p=0.59$ ). Normal swallowing function was observed in 60% of patients, intermittent dilatation required in 29% of the patients and 11% patients continued with PEG feeding.

**Conclusions:** High dose rate endoluminal brachytherapy combined with external beam radiation with or without chemotherapy can be safely used as an effective boost. The local control rate and the functional results are encouraging.

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POSTER

# **Aminothiols WR-1065, the active metabolite of Amifostine (Ethyol), protects in vitro lens epithelial cells against X-ray exposure**

Y. Belkacemi<sup>1</sup>, P. Rat<sup>1</sup>, G. Piel<sup>3</sup>, D. Pasquier<sup>1</sup>, B. Castelain<sup>1</sup>, J.-M. Warnet<sup>2</sup>, E. Lartigau<sup>1</sup>. <sup>1</sup>Oscar Lambret Center, Radiation Oncology, Lille, France; <sup>2</sup>CHNO XV-XX, Pharmacy & Cell Pharmacotoxicology Unit, Paris XII, France; <sup>3</sup>MedPass International, Biostatistics, Paris XVII, France

**Background:** Lens epithelium disorganization is considered as one of the radiation-induced cataract cytopathomechanisms. Epithelial cell death is involved in cataractogenesis process after X-ray irradiation. Our objective was to test the capacity of aminothiols WR-1065, active metabolite of amifostine (or WR-2721) to protect *in vitro* bovine lens epithelial cells against X-ray exposure.

**Material and methods:** WR-1065 was used for cultures pretreatment at a concentration of 20  $\mu$  M. A single dose of 10 Gy was delivered using a dose rate of 2 Gy/min. To evaluate radioprotective effect we used cold light cytofluorimetric assays. Cell viability and membrane damage were evaluated with neutral red probe assay. To evaluate cell proliferation, we used Hoechst 33342 probe (HO) assay followed by an inverted fluorescence microscopic examination for nuclear apoptotic morphology changes of the HO-labeled cells. Monobromobimane probe assay was used for GSH pool evaluation.

**Results:** Twenty-four hours after irradiation, WR-1065 pretreated cells showed a significant increase of the GSH levels, which was associated with an improvement of cell viability, a decrease of the HO fluorescence and a reduction of the proportion of cells with nuclear changes related to apoptotic cell death. The difference was also significant at 48h and 96h after exposure. Statistical analyses showed a highly significant difference between irradiated and control cultures.

**Conclusion:** In this study, using cold light cytofluorimetric assays, we showed that WR-1065, can protect *in vitro* lens epithelial cells from X-ray injury. The fluorimetric assays revealed better cell viability, fewer nuclear changes related to apoptosis and an increase of the GSH pool in the pretreated cells as compared to non pretreated cells. Thus, we postulate that amifostine is potentially interesting in the view of lens protection against radiocataractogenesis.

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POSTER

# **Radiotherapy vs. radiotherapy + chemotherapy of advanced cervical cancer (Ib - IVa): Regression of tumour and early sequelae**

S. Cikiric, S. Stupar-Petrovic, V. Plesinac-Karapandzic, I. Marjanov, Lj. Rudan, S. Colakovic, M. Saric, B. Mihajlovic. *Institute for Oncology and Radiology of Serbia, Department of Radiotherapy, Belgrade, Serbia*

A prospective randomised Study of 200 patients with advanced cervical cancer (st. Ib-IVa) treated with either radiotherapy alone (RT group) or radiotherapy + chemotherapy (RT + CH group) was started at the beginning of May, 2002 and the last patient of this series was treated in March 2003. (Project N° 1683 of Ministry of Science, Technology and Development of Rep. Serbia). The aim of this study is to show comparison of results of treatment of advanced cervical cancer using either RT or RT + CT.

Clinical material of 200 cervical cancers randomised in two groups: RT 98 (49%) pts and RT + CT 102 (51%) pts. Distribution of patients by stages (FIGO), histopathological type (and gradus) and age was very similar in both groups.

Treatment regimes were:

1. RT group: - CBT 46Gy/22 fractions, 2 parallel opposite fields without central Pb shields + HDR brachytherapy 5x7 Gy/A (Ut. tube + 2 vag. ovoids)
2. RT + CT group: RT vs. first group + CT using cisplatin (5 cycles during radiotherapy, one's week).

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POSTER

# **Evaluation of polymer gels and laser-beam optical CT scanner as a 3-D dosimeter for IMRT**

W. Cheng-Shie<sup>1</sup>, Y. Xu<sup>1</sup>, M. Maryanski<sup>1</sup>, M. Maryanski<sup>2</sup>. <sup>1</sup>Columbia University, Department of Radiation Oncology, New York, USA; <sup>2</sup>MGS Research Inc., Madison, USA

**Purpose/objective:** Dose distributions generated from IMRT treatment planning present high dose gradient regions in the boundaries among target and surrounding critical organs. Dose accuracy in these areas can be critical, and may affect the treatment. With the increasing use of IMRT in radiotherapy, there is an increased need for a dosimeter that allows high resolution, precise, and accurate determination of 3-dimensional dose distributions. In this study, 3-D dose verification for IMRT has been implemented using polymer gel dosimeters and a laser-beam optical CT scanner.

**Material and Methods:** A 17 cm diameter x13 cm height plastic cylinder filled with BANG<sup>®</sup> polymer gel, modified to optimal dose-response characteristics, was used for IMRT dose verification. The cylindrical gel phantom was immersed in a 24x24x20 cm water tank for IMRT irradiation. The irradiated gel sample was then mounted in the prototype optical CT scanner developed by MGS Research Inc., utilizing a single He-Ne laser beam and a single photodiode detector. Similar to the CT process, filtered backprojection was used to reconstruct the 3-D dose distribution. The gel was scanned using 20x20 cm field of view and 200x200 image matrix, which produced 1 mm pixel resolution. Image slices were acquired 1mm apart. The dose distributions measured from the gel was compared with those from the IMRT treatment planning system. For comparative dosimetry, a solid water phantom of 24x24x20 cm, having the same geometry as the water tank for the gel phantom, was used for radiographic film and ion chamber measurements.

**Results:** Comparison of planar dose distributions among gel dosimeters, film, and a treatment planning system showed that the isodose lines agreed to within 2 mm on transverse and coronal slices. Absolute point-dose verification was performed at 5 different points, varying from 65% to 110% of the prescribed dose. Comparing ion chamber measurements and the dose calculation from the treatment plan, the agreement was found to be within 3%.

**Conclusions:** Polymer gel dosimeters and laser-beam optical CT scanner provides a high resolution, accurate, 3-dimensional tool for IMRT dose distribution verification.

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POSTER

# **Circulating lipid peroxide, glutathione and nitric oxide levels in cancer patients irradiated on different anatomic fields**

D. Unsal<sup>1</sup>, M. Akmansu<sup>1</sup>, C. Ozer<sup>2</sup>, B. Gonul<sup>2</sup>, H. Bora<sup>1</sup>. <sup>1</sup>Gazi University Faculty of Medicine, Department of Radiation Oncology, Ankara, Turkey; <sup>2</sup>Gazi University Faculty of Medicine, Department of Physiology, Ankara, Turkey

**Background:** Irradiation is known to produce free radicals that damage cells. The effect of ionizing radiation on surrounding normal cells may differ in various irradiated sites. The aim of this study was both to evaluate the effect of radiotherapy (RT) on plasma malondialdehyde (MDA) level as the last step of lipid peroxidation, glutathione (GSH) and nitric oxide (NO) levels of cancer patients treated on different RT field localizations, and to compare the results with control subjects.

**Material and Methods:** A prospective, controlled study was designed to examine the influence of different irradiation portals. The study design was approved by the Ethics Committee of our University. The effect of RT on MDA, GSH and NO were evaluated in the irradiated cancer patients (n=89), mean age 51.24 years and control subjects (n=33), mean age 52.61 years. The grouping of the irradiation procedure was: Group 1 (n=12) head & neck RT, group 2 (n=13) thoracic RT, group 3 (n=32) breast RT, group 4 (n=17) abdominal RT, group 5 (n=15) pelvic RT. There were two blood samples collected from patients before receiving radiotherapy and the next day after the completion of the fifth week of radiotherapy. Serum was separated by centrifugation and stored at -20 °C until further assay. MDA and GSH levels were measured by spectrophotometrical, and NO levels were measured by Gress' method.

**Results:** When compared to control, MDA levels of all cancer patients before irradiation was initiated were found significantly higher in all groups (Mann Whitney U,  $p<0.05$ ). After RT, the levels of MDA were found significantly increased by thoracic, breast, abdominal and pelvic irradiation (Wilcoxon signed rank test,  $p<0.05$ ). Although pretreatment NO levels of all cancer patients in all groups were found significantly higher than control

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.

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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 ( $>10\text{mm}$ ). 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 be 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.

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POSTER

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

D. Mileusnic, B. Pantic. <sup>1</sup> Military Medical Academy, Department of Radiotherapy, Belgrade, Yugoslavia

**Purpose:** To compare the isodose distribution of three radiotherapy techniques for locally advanced maxillary sinus 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 fourteen patients with T3-T4, N0, M0 maxillary sinus carcinoma were acquired and transferred to treatment planning system. A conventional 2D treatment plans with classically 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 contoured 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 assessed 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 ( $D_{\text{max}}$ :  $p < 0.05$ ;  $D_{\text{aver}}$ :  $p < 0.01$ ;  $D_{\text{min}}$ :  $p < 0.05$ ;  $V_{90}$ :  $p < 0.05$  and  $V_{95}$ :  $p < 0.01$ ) and 3D-NS vs. 3D-S technique ( $D_{\text{min}}$ :  $p < 0.05$ ;  $V_{90}$ :  $p < 0.05$  and  $V_{95}$ :  $p < 0.01$ ) 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  $D_{\text{max}}$  for ipsilateral retina comparing with 3D-S technique, while (because of beams direction) the level of  $D_{\text{max}}$  for optic nerve was increased (but in acceptable range) with 3D-NS technique.

**Conclusion:** 3D planning of radiotherapy for locally advanced maxillary sinus 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 contiguous uninvolved healthy tissue structures.

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POSTER

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

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

**Objective:** Combined modality treatment, including radiotherapy and cisplatin, is now frequently and successfully 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  $\mu\text{M}$ ) 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.

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POSTER

### Evaluation of quality assurance procedure in brain tumors radiotherapy in children

K. Ficek<sup>1</sup>, S. Blamek<sup>1</sup>, L. Miszczyk<sup>1</sup>, K. Slosarek<sup>2</sup>. <sup>1</sup> Center, Radiotherapy Department, Gliwice, Poland; <sup>2</sup> 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