Conclusion: We demonstrate that neural stem cells in the ventricle-hippocampal region are highly radiosensitive and that apoptosis of the stem cells could be an initial step of radiation injury. Ionizing radiation accelerates differentiation of stem cells into oligodendrocyte lineage leading to myelin synthesis disorder. These evidences pave the way for the understandings of a mechanism of radiation-induced leukoencephalopathy.

757 POSTER

Intraluminal application of potential radioprotectors in an animal model of localized hypofractionated small bowel irradiation

K.K. Richter[1], A. Meyer[1], T. Wedel[2], B. Erdmann[3], J. Fuller[3], T. Wendt[3], H. Kosmehl[4], H. Schubert[5], J. Scheele[1]. [1] *Friedrich-Schiller-University, Surgery, Jena, Germany;* [2] *University Luebeck, Anatomy, Luebeck, Germany;* [3] *Friedrich-Schiller-University, Radiooncology, Jena, Germany;* [4] *Friedrich-Schiller-University, Pathology, Jena, Germany;* [5] *Friedrich-Schiller-University, Veterinary Medicine, Jena, Germany*

Purpose: The risk of normal intestinal toxicity is a major dosis-limiting factor during radiation therapy for abdominal and pelvic malignancies. Investigations have been directed toward increasing normal tissue tolerance by using radioprotectors, however, intraveneous administration of potential radioprotectors, i.e. amifostine, has produced limiting nausea and vomiting. The presented animal model was developed for intraluminal application of potential radiation biology modifiers and localized fractionated small bowel irradiation.

Methods: Fourty two male Sprague-Dawley rats were orchiectomized and a 5 cm segment of small bowel was sutured to the inside of the scrotum to form an artificial "scrotal hernia". In addition, a proximal Bishop-Koop ileostomy was fashioned for intraluminal drug application; small intestine was re-anastomosized end-to-side using 6-0 absorbable interrupted sutures. After 4 weeks postoperative recovery small intestine in the scrotal hernia was sham-irradiated or exposed locally to hypofractionated orthovoltage radiation of daily 5 x 5 Gy or 5 x 7,5 Gy. In treatment groups 10 min. before irradiation 50 mg Ethyol (Amifostine) dissolved in 9M buffer was administered intraluminally. Specimens of sham-irradiated or irradiated intestines were procured at 2 weeks after the end of irradiation and assessed for morphologic changes by semiquantitative histopathology and for extracellular matrix-associated pan-TGFbeta by immunohistochemistry. In addition, the enteric nerve system (ENS) was assessed using electron microscopy.

Results: Surgery and anaesthesia related mortality rates were 5% and 2%, respectively. Irradiated animals exhibited characteristic dose-dependent intestinal mucosal denudation, inflammation, subserosal thickening, differences between the irradiated groups were significant (p=0.02). Amifostine-treated animals in the 7.5 Gy group showed a slight but not significant reduced intestinal injury at 2 weeks than irradiated animals treated with buffer. Using electron microscopy irradiated specimens exhibited characteristic alterations of the ENS.

Conclusion: This animal model allows the application of fractionated small bowel irradiation in combination with local testing of potential radioprotectors locally. Amifostine and other locally acting radioprotectors should undergo further testing, particular as modifiers of chronic intestinal radiation toxicity.

758 POSTER

Chromosomal damage and survival of keratinocytes and fibroblasts after irradiation with 200 kV and 25 kV X-rays

D. Slonina[1], K. Speki[2], K. Brankovic[2], A. Panteleeva[3], W. Doer[2]. [1] *Centre of Oncology, Laboratory of Radiation Biology, Krakow, Poland;* [2] *Technical University, Medical Faculty Carl Gustav Carus, Dresden, Germany;* [3] *Forschungszentrum Rossendorf, Dresden, Germany*

Purpose: A relative biological effectiveness (RBE) of 1 is generally accepted for soft X-rays (25-30 kV), which are applied in diagnostic radiology (mammography). However, it has been shown, that soft X-rays can be more effective in cell killing and chromosomal damage. The present study was initiated to define biological effects of low-energy X-rays in vitro.

Methods: Experiments were performed with 25 kV X-rays and 200 kV reference X-rays on neonatal human keratinocytes (HEKn), human fibroblasts (HFIB) and NIH/3T3 mouse fibroblasts. Cell survival was studied with graded doses in a clonogenic assay, chromosomal damage in a micronucleus (MN) assay.

Results: The surviving fraction at 2 Gy for keratinocytes was 46±5% after 200 kV and 33±11% after 25 kV X-rays. Linear-quadratic cell survival analysis yielded a=0.31±0.03 Gy-1 and b=0.048±0.011 Gy-2 for 200 kV and a=0.40±0.10 Gy-1 and b=0.048±0.054 Gy-2 for 25 kV. For 3T3 fibroblasts SF2 of 53±3% after 200 kV and 61±18% after 25 kV were observed. Values of a=0.24±0.02 Gy-1 and b=0.022±0.002 Gy-2 for 200 kV and a=0.10±0.05 Gy-1 and b=0.070±0.010 Gy-2 for 25 kV X-rays were derived. The induction of binucleated (BN) cells in the MN assay was highly dependent on the cell line studied, but independent on radiation quality. Compared to the effect of conventional, 200 kV X-rays, 25 kV X-rays resulted in an increased number of chromosomal damages expressed as either the percentage of BN cells with micronuclei (%BNC + MN) or the number of micronuclei per BN cell (MN/BNC).

Conclusion: Cell survival after 25 kV and 200 kV X-irradiation was similar, although for 3T3 fibroblasts, a reduction in survival at higher doses was observed after 25 kV X-rays. Induction of micronuclei after irradiation with 25 kV X-rays was significantly higher than with 200 kV, resulting in a RBE value of about 1.2. This indicates a higher potential of the soft X-rays for the induction of genetic damage.

759 POSTER

Tumor interstitial fluid pressure in patients: possible correlation with tumor size

M. Cho[1,2], J. Kim[1,2], I. Lee[3], J. Jang[1], K. Kim[1]. [1] *Chungnam National University, College of Medicine, Therapeutic Radiology, Taejon, Korea;* [2] *Chungnam National University, Cancer Research Institute, Taejon, Korea;* [3] *University of Pennsylvania, School of Medicine, Department of Radiation Oncology, Philadelphia, U.S.A*

Purpose: Interstitial fluid pressure (IFP) is determined by the volume of free interstitial fluid and the distensibility of the interstitium. Normal tissues have low vascular permeability and an extensive lymphatic network, and therefore contain only small quantities of interstitial fluid at low pressure. IFP in normal tissues is between -5 and +5 mmHg. Malignant tumors are very permeable and lack functional lymphatics, which allows free fluid to accumulate in the interstitium, producing a high tumor interstitial fluid pressure (TIFP). A high TIFP may be associated with hypoxia and poor prognosis in radiotherapy. TIFP may increase with tumor size. In this study, we evaluated whether TIFP is correlated with tumor size.

Materials and Methods: From August 1998 to December 2000, we measured TIFP using a modified wick-in-needle technique in 33 biopsy-proven uterine cervical cancer patients and 33 primary or metastatic head and neck cancer patients in whom the tumor was accessible by direct inspection and palpation and was sufficiently thick (>1 cm) to permit accurate needle placement. Blood pressure was checked before TIFP measurement. Tumor size was measured by clinical and radiological methods.

Results: In cervical cancer, the mean TIFP was 29.1 mmHg and had no significant relationship with tumor size (p = 0.59). In head and neck cancer, the mean TIFP was 26.5 mmHg and was significantly related to tumor size (p = 0.03).

Conclusion: The mean TIFP was elevated at 29.1 mmHg in cervical cancer and 26.5 mmHg in head and neck cancer. TIFP was significantly related to tumor size in head and neck cancer.

This study was supported by a 1998 Nuclear R & D Program from the Ministry of Science and Technology of Korea.

760 POSTER

Influence of percutaneous radiotherapy on skin microcirculation

J. Scheiderbauer[1], A. Schlez[2], S. Braun[2], L. Plasswilm[1], M. Bamberg[1], M. Juenger[2]. [1] *University of Tuebingen, Radiooncology, Tuebingen, Germany;* [2] *University of Tuebingen, Dermatology, Tuebingen, Germany*

Purpose: Acute and chronic skin reactions represent serious side effects in radiotherapy (RT). Both are accompanied by histologically proven changes of capillary vessels. The aim of this investigation was to show evidence for these changes under in-vivo-conditions.

Methods: Morphologic modifications of the nutritive skin capillaries have been investigated by means of the capillary microscopy in eight irradiated patients with different malignant tumours. Treatment has been delivered by linear accelerator with 6 or 15 MV photons. Measurements were performed before, during, at the end of treatment and twice in follow up. An investigation of the deeper plexus of thermal regulation of the skin took place with the laser doppler flowmetry (LDF). Investigation areas were the irradiated field and un-irradiated skin (controls). Acute and chronic skin reactions were scored by RTOG/EORTC toxicity criteria respectively LENT/SOMA tables.

Results: An edema formation was shown in all patients during RT leading to reduced skin transparency. Therefore capillary density could be