829 POSTER

EFFECT OF HYPOXIC CELL SENSITIZATION ON GLUCOSE METABOLISM OF SQUAMOUS-CELL CARCINOMA

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Overcoming hypoxic radioresistance with chemical sensitizers has potential to improve therapeutic outcome of head and neck cancer. Squamous-cell carcinoma cell line from a patient with lingual cancer (UT-SCC-5) was exposed to moderate (1.5% pO_2) and severe (0% pO_2) hypoxia, known to increase *in vitro* uptake of 2-[^{3}H]fluorodeoxyglucose (FDG) by neoplastic cells. [^{3}H]FDG uptake in well oxygenated (20% pO_2) UT-SCC-5[2] -cells incubated with 5 mM of misonidazole (MISO) or nimorazole (NIMO) increased by 101 ± 41% and 84 ± 23%, respectively. Incubation of UT-SCC-5 in 1.5% pO_2 resulted in a decrease of [^{3}H]FDG uptake by 6 ± 4% in the presence of 5 mM of MISO while it increased by 43 ± 14% with 5 mM of NIMO. In 0% pO_2 both drugs showed a decrease of 58 ± 6% (MISO) and 6 ± 18% (NIMO), respectively. These *in vitro* studies indicate differential modification of glucose metabolism by two well known radiosensitizers in air and hypoxia. Based on these observations, we suggest that imaging of head and neck cancer with 2-[^{18}F]FDG and positron emission tomography (PET) may assist in evaluation of *in vivo* effects of hypoxic cell sensitizers.

830 POSTER

THE ROLE OF SUPEROXIDE DISMUTASE IN PROTECTION AGAINST RADIATION-INDUCED DNA DAMAGE

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Heritable variation in cellular radiosensitivity is believed to be an important determinant of normal tissue responses to radiation. There is increasing evidence that the initial level of DNA damage induced determines this cellular radiosensitivity. The superoxide dismutase genes have been shown to influence cellular radiosensitivity through their effects on free-radical damage. In this study we have examined the effect of inherited mutations in the Cu/Zn superoxide dismutase on DNA damage induction following ionizing radiation treatment.

We have examined lymphoblastoid cell lines from normal individuals and patients with Familial Amyotrophic Lateral Sclerosis (FALS)—recently identified as having Cu/Zn SOD gene mutations. Radiation-induced DNA damage has been measured in these cell lines using pulsed-field gel electrophoresis (PFGE).

A two-fold range of DNA damage induction was found between cell lines but this was unrelated to the mutations in the SOD1 gene. These data suggest that the SOD1 gene does not influence DNA damage induction but its influence on other aspects of cellular radiosensitivity require further evaluation. Despite the lack of correlation with Cu/Zn SOD mutations the wide range in DNA damage induction shown here has not been previously reported in lymphoblastoid cell lines and the implications of this on radiotherapy need to be considered.

831 POSTER

EFFECTS OF IONIZING IRRADIATION AND ADRENERGIC STIMULATION ON GENE EXPRESSION PATTERN IN RAT SUBMANDIBULAR GLANDS

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Radiotherapy administrated to patients with head and neck malignancies often results in severe xerostomia. We evaluated the expression of early response proto-oncogenes (c-fos and jun-B), tissue specific genes (proline rich protein (PRP) and kallikrein), and proteolysis linked ubiquitin gene following exposure to 15 Gy irradiation and/or adrenergic stimulation of the rat submandibular gland. We observed that the expression of the genes whose regulation is associated with DNA damage (i.e. jun-B and c-fos) was enhanced by irradiation or the combination of irradiation and isoproterenol administration. In contrast, the expression of genes associated with the routine functional integrity of the cell (i.e. kallikrein, ubiquitin and PRP) was uneffected. These findings, in addition to delayed gland dysfunction, leaves us to believe that irradiation induced injury to the submandibular glands is to be attributed to reproductive stem cell death which may be obliterated in some part in a clinical setting.

832 POSTER

ACUTE RADIATION-INDUCED THYROIDITIS—A PROSPECTIVE STUDY

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Purpose: We prospectively studied acute radiation-induced thyroid dysfunction by performing thyroid function tests.

Materials and methods: The subjects were 28 patients who underwent neck irradiation incidentally including the thyroid for various malignancies. The total dose absorbed by the thyroid was 4500–5000 cGy. Thyroid function tests included serum thyroid stimulating hormone (TSH), free triiodothyronine (T3), and free thyroxine (T4). These data were obtained before irradiation, at 40 Gy irradiation, and 3 and 6 months thereafter.

Results: Mean TSH levels were 1.57, 0.66, 1.34, and 6.23 μU/ml at preirradiation, 40 Gy irradiation, and 3 and 6 months after irradiation, respectively. The decrease in TSH levels at 40 Gy was significant (P = 0.0001, Wilcoxon signed-rank test). TSH levels significantly increased thereafter until 6 months (40 Gy vs 3 months:P = 0.001, 3 months vs 6 months:P = 0.028). Mean T4 levels increased from 1.13 to 1.21 ng/ml during 40 Gy irradiation (P = 0.02).

Conclusion: The elevation of T4 and decrease in TSH observed at the time of irradiation was attributed to acute thyroid follicular cell destruction by irradiation.

833 POSTER

NEUTRON CAPTURE POTENTIATION: HOW TO GET SOME SELECTIVITY IN A FAST NEUTRON BEAM?

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Neutron captures on ^{10}B may be a neat way to provide some selectivity in a fast neutron beam: when the neutrons are thermalized in the tissue, they produce nuclear reaction with ^{10}B nuclei, releasing energetic α particles and Li ions. Provided that a sufficient amount of ^{10}B may be carried with a specific molecule inside tumoral cells, a very efficient component of irradiation can be added.

Tumors like glioblastomas, soft tissues sarcomas or melanomas, which are highly radioresistant, may benefit of this potentiation to obtain better local control, while sparing more the normal tissues.

Results of tumor targeting with boronated compounds, of dosimetry and radiobiology in our fast neutron beam will be presented.

834 POSTER

THE INFLUENCE OF CELL DENSITY DEPENDENT PLATING EFFICIENCY ON CLONOGENIC ASSAYS

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To measure cell survival after ionizing radiation, clonogenic assays are considered the standard. Survival is expressed in plating efficiency reduction. However for some cell lines we discovered that plating efficiency was strongly dependent on the numbers of cells seeded; with increasing numbers of cells the plating efficiency decreases. Data were taken from human melanoma cell lines transfected with oncogenes c-myc and N-ras and normal human fibroblasts, that had been tested for *in vitro* radio sensitivity. For each dose a range of cell numbers was taken and survival was calculated based on (a) the total data available, (b) data from lowest number of colonies per dish, where a linear relationship between cell numbers and plating efficiency exists and (c) the highest number of colonies per dish, as can be statistically more interesting.

It will be shown that if plating efficiency is not correctly determined, that the interpretation of the data can lead to wrong estimation of survival. It is concluded: