with chemotherapy. Each patient received 3 cycles of treatment before continuing to radiotherapy of 70 Gy (fractionated) as local treatment.
Results: Between January 2000 and December 2003, a total of 69 patients were enrolled and assessable for response and toxicity analysis. The median age was 55 years (age range 45–70 years). The anatomical sites were oral cavity (45%), nasopharynx (35%) and larynx (20%). Overall response rate was 96% with complete response seen in 42 patients (61%) and partial response in 24 patients (35%). The remaining patients (4%) showed stable disease. The median time for follow-up was 45 months. The most common hematological side effects were neutropenia (35 patients; 51%) out of which G3/4 was found in 10 patients. The non-hematological events were vomiting (28 patients; 41%) and stomatitis (10 patients; 14%). There were no treatment related deaths.
Conclusion: For treatment of locally advanced SCCHN, docetaxel in combination with cisplatin and 5-FU may be an effective regimen with a manageable toxicity profile.

1096 PUBLICATION

Tamoxifen as a novel chemotherapeutic agent treating anaplastic thyroid cancer.

J. O'Neill, B. O'Neill, C. Condron, M. Walsh, D. Bouchier-Hayes.
The Royal College of Surgeons in Ireland, Dept of Otolaryngology and Surgery, Dublin, Ireland

Introduction: Anaplastic Thyroid Cancer (ATC) is a highly aggressive rare neoplasm with a dismal prognosis. It represents 2% of all thyroid cancers with a mean survival of 3–7 months. The majority of ATC patients develop metastases during their illness hence there is an essential role for systemic chemotherapy. Doxorubicin, cisplatin and paxlitaxel to date offer poor chemotherapeutic response.
Method: We have investigated the anti-proliferative effects using colorometric dimethyl-thiazol-diphenyltetrazolium bromide (MTT), pro-apoptotic effects was investigated using flow cytometry and annexin V and anti-invasive properties using Matrigel invasion assays at varying concentrations of tamoxifen on anaplastic thyroid carcinoma cell line Cal-62.

Results:

Tamoxifen	Control	1 μg/ml	2 μg/ml	5 μg/ml	10 μg/ml
Proliferation	100	97±1.07*	93±0.75*	64±1.07 **	23±1.07**
Apoptosis	4.7±0.46	11.2±2.39	26.4±14*	24.8±2.19	22.9±6.89
	Control	**Tamoxifen**	**Vegf**	**Tamx + Vegf**	
Migration	95.8±3.1	0*	124±3.15**	45.6±3.14**	

P < 0.05 vs control Anova Scheffe post hoc analysis

Conclusion: These data suggest tamoxifen warrants further investigation as a novel therapeutic agent in the treatment of Anaplastic Thyroid Cancer

1097 PUBLICATION

Lovastatin and X-irradiation induced redistribution in cell cycle and growth inhibition of FaDu cells in vitro

D. Gabrys[1,2], A. Dorfler[2], M. Baumann[2,3]. [1]*Center of Oncology Maria Sklodowska-Curie Memorial Institute, Department of Radiation Oncology, Gliwice, Poland;* [2]*Medical Faculty Carl Gustav Carus University of Technology, Department of Radiation Oncology, Dresden, Germany;* [3]*Medical Faculty Carl Gustav Carus University of Technology, Experimental Centre, Dresden, Germany*

Background: Identification of drugs which selectively radiosensitise tumours may have important clinical benefits for cancer patients. Such a drug might be lovastatin, a well known antihypercholsterolemic agent which specifically inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Lovastatin was shown to have the ability to induce growth arrest in the G_0/G_1 phase of the cell cycle in several tumour-derived cell lines. Lovastatin has been evaluated in combination with different chemotherapeutic drugs but little is known about its combination with irradiation. The aim of this project is to investigate the effects of lovastatin and lovastatin combined with X-radiation on the cell cycle distribution and growth of FaDu cells *in vitro*.
Material and methods: The human hypopharyngeal squamous cell carcinoma cell line FaDu was used in all experiments. Lovastatin was dissolved in ethanol. Proliferation was determined by cell counts, cell cycle distribution by flow cytometry. Clonogenic cell survival was determined using colony formation and dilution assays after incubation of cells for 72 hours with lovastatin. For experiments combined with irradiation, cells were irradiated 36 hours after seeding and then treated with lovastatin or cells were irradiated after incubation with lovastatin for 24 – 72 hours.
Results: Lovastatin inhibited cell proliferation in a dose-dependent manner. Combined treatment (4 Gy X-rays and 25 μM lovastatin) showed greater effects on proliferation than both treatments alone. Lovastatin (5 μM – 50 μM) leads to an increased proportion of cells in the G_0/G_1 phase (control 39%, 50 μM lov 69%), a decreased number in S-phase (control 41%, 50 μM lov 17%), and increased apoptosis. Irradiation with 4 Gy X-rays caused an increase in the number in the G_2/M phase. This was not significantly modified by addition of 25 μM of lovastatin. Lovastatin reduced colony formation dose-dependently. Also here the effects of combined treatment were greater than each modality alone.
Conclusion: Lovastatin, in a dose-dependent manner, decreases cell proliferation and clonogenic survival and increases apoptosis. Effects on proliferation are caused by G_0/G_1 arrest. Radiation combined with lovastatin decreases proliferation and clonogenic survival to a greater extent than lovastatin alone.

1098 PUBLICATION

Serum ubiquitin levels and antioxidan system in patients with solid tumors treated with radiotherapy

A. Bilgihan[2], Y. Guney[1], M. Akmansu[3], H. Bora[3], C. Aybars[4]. [1]*Ankara University School of Medicine, Radiation Oncology, Ankara, Turkey;* [2]*Gazi University School of Medicine, Biochemistry, Ankara, Turkey;* [3]*Gazi University School of Medicine, Radiation Oncology, Ankara, Turkey;* [4]*Gazi University School of Medicine, Immunology, Ankara, Turkey*

Background: The ubiquitin-proteosome system is a major non-lysosomal proteolytic pathway in eukaryotic cells. Ubiquitinated proteins are degraded by an ATP dependent 26S proteosome complex. Ubiquitin, which can conjugate with cellular proteins, is classified into two forms: free ubiquitin and multiubiquitin chains. The multiubiquitin chain acts as a signal to induce degradation of the target proteins by 26S proteasome.
The ubiquitin-proteosome pathway clearly represents an important area of research in cancer biology. On the other hand experimental investigations have showed the relation between ionizing radiation and free oxygen radicals. The aim of this study was to assess the level malondialdehyde (MDA), selenium (Se), ubiquitin (Ub) and activities of superoxide dismutase (SOD) in advanced head-neck cancer patients and compare the results of these parameters which were detected at the beginning, in the middle and at the end of the radiotherapy.
Methods: Sixty patients with advanced epidermoid head and neck carcinoma and sixty healthy cases as the control group were enrolled into the study. Patients were treated with radiotherapy alone. Serum was obtained from venous blood drawn at the beginning of radiotherapy, in the middle of radiotherapy and at the end of the radiotherapy. The MDA, Se, Ub levels and SOD activities in sera were quantified.
Results: Higher serum levels of MDA, lower serum activities of SOD and lower levels of Se and Ub were detected in patients with advanced cancer of head-neck without surgical therapy in comparison to the healthy volunteers. SOD activity slightly decreased during the treatment. Activities of SOD at the end of the treatment significantly decreased as compared to the results of the beginning treatment. The levels of MDA and Se decreased during the treatment but it was not significant. The levels of Ub altered during treatment. Ub markedly decreased in the middle of the treatment compared with the results of the beginning of treatment. The levels of Ub returned the values which were detected at the beginnig of the treatment.
Conclusion: This study demonstrated that serum SOD, MDA, Ub and Se analysis might serve as nonspecific markers in the assessement of oxidative stres response to radiotherapy in advanced head-neck cancer.

1099 PUBLICATION

Immunohistochemical markers PCNA-LI and Ki-67, and DNA index in patients with parathyroid carcinoma

F. Lumachi[1], F. Marino[2], M. Iacobone[1], G. Favia[1]. [1]*University of Padua, School of Medicine, Endocrine Surgery Unit, Department of Surgical & Gastroenterological Sciences, Padova, Italy;* [2]*University of Padua, School of Medicine, Department of Pathology, Padova, Italy*

Background: Parathyroid carcinoma (PC) is an uncommon cancer. Unfortunately, histopathological distinction between PC and parathyroid adenoma is still difficult and, moreover, the clinical outcome of patients varies widely. The aim of this study was to assess the usefulness of antiproliferating cell nuclear antigen labeling index (PCNA-LI), Ki-67 antigen, and tumor nuclear DNA index (DI) in patients with parathyroid carcinoma.
Patients and Methods: Paraffin-embedded archivial tissue sections from 15 patients (11 men, 4 women, median age 65 years, range 30–68 years) with confirmed PC who died of the disease were reviewed. Specimens were stained by using streptavidinbiotin-peroxidase complex standard technique

and monoclonal antibodies anti-PCNA and anti-Ki-67 (MIB-1). The DNA flow cytometry to determine DI was also used.
Results: The greatest diameter (size) of the tumor measured by the pathologist was 29±9 mm. The mean survival of patients was 47±37 years (median 29 months, range 21–146). Diploid (DI = 1) and aneuploid (DI > 1) tumors were found in 4 and 11 cases, respectively. The median PCNA-LI was 13% (range 2–70%), and the median MIB-1 value was 11% (range 3–65%). The survivals of patients with diploid and aneuploid tumors were 74±58 months and 34±18 months (p = 0.21), respectively. There was a linear relationship between PCNA-LI and MIB-1 (R = 0.93, p < 0.01), but no correlation between age and survival (R = 0.08, p = 0.78) was found. Moreover, there was no correlation between survival and DI (R = 0.17, p = 0.55), PCNA-LI (R = 0.07, p = 0.72), and MIB-1 (R = −0.05, p = 0.86).
Conclusions: PCNA-LI, MIB-1, and DI may be useful in confirming the diagnosis of malignancy, but they are of little value in predicting the clinical outcome of patients with PC.

1100 PUBLICATION

Expression of cystein proteases cathepsin B in inoperable squamous cell carcinoma of the head and neck

I. Oblak[1], P. Strojan[1], N. Gale[2], L. Mid[3]. *Institute of Oncology, Department of Radiotherapy, Ljubljana, Slovenia; [2]Institute of Pathology, Medical Faculty, Ljubljana; [3]University Medical Center, Dept. of Otorhinolaryngology and Cervicofacial Surgery, Ljubljana*

Background: To determine the expression profile of CB and its prognostic value.
Patients and Methods: The expression of CB was determined on the tissue sections of primary tumors from 75 patients with inoperable SCCHN, treated with concomitant radiochemotherapy with Mitomycin C and Bleomycin. The data available for each patient were age, sex, performance status, tumor site, UICC TNM stage, histopathological grade, response to therapy and survival. The expression of CB was determined immunohistochemically using commercially available antibodies from KRKA D.D., Novo Mesto, Slovenia. The intensity of immunohistochemical reaction was scored as follows: G 0 = 0% tumor cells with positive nuclear reaction; G 1 = 1 – 10%; G 2 = 10 – 50%; G 3 = >50%.
Results: The expression of CB was scored as: G 1: 2 pts (3%); G 2: 8 pts (11%); G 3: 65 pts (86%). The grade of expression (grade 1+2 vs. Grade 3) correlated negatively with the primary tumor subsite (posterial wall vs. others, p = 0.001), and positively with the response to therapy (partial response/ no change vs. complete response locoregionally, p = 0.05), disease progression status (yes vs. no, p = 0.04) and with the deaths for oropharingeal carcinoma (yes vs. no, p = 0.01) In all patients, staining intensity did not correlate with survival probability. However, significantly higher disease-free survival (DFS) and disease-specific survival (DSS) rates at 5 years were observed in the subgroup of patients with N+ regional disease (n = 59) and with less intensive nuclear reaction to CB: DFS 70% vs. 36%, p = 0.07); DSS 84% vs. 36%, p = 0.03. On multivariate analysis, performance status, radiotherapy dose, and UICC TNM stage of the disease, but not CB grade of staining, were identified as independent prognostic factors for DFS and DSS.
Conclusions: Predictive value of staining intensity of CB for response to therapy warranted further investigation, whereas its prognostic value seemed to be limited to N+ subgroup.

Imaging

Oral presentations (Thu, 3 Nov, 8.30–10.30)
Imaging

1101 ORAL

Monitoring of tumor oxygenation changes in head and neck carcinoma patients breathing a hyperoxic hypercapnic gas mixture (carbogen) with a non-invasive MR technique

M. Kotas[1], P. Schmitt[2], P. Jakob[2], M. Flentje[1]. *[1]University of Wuerzburg, Department of Radiation Oncology, Wuerzburg, Germany; [2]University of Wuerzburg, Department of Experimental Physics, Wuerzburg, Germany*

Background: Influenced by tumor blood flow, tumor tissue perfusion and oxygen supply, increased tumor tissue oxygen levels may improve the radiosensitivity of tumors. Therefore a non-invasive oxygenation-sensitive MR technique may be of prognostic value and useful to preselect patients for individual treatments using hyperoxic gas mixtures like carbogen (5% CO_2 and 95% O_2) or carbogen "light" (2% CO_2 and 98% O_2).
Material and Methods: A total of 14 patients with histologically proven head and neck carcinoma were investigated on a 1.5T clinical MR scanner. Over the course of the examination, different breathing gases were administered via a soft face mask system (3min air, 6min carbogen "light", 4min air, 3min oxygen). A multi-gradient-echo sequence was used for quantification of the apparent transverse relaxation time T2* which is sensitive to oxygenation changes. A series of 32 acquisitions was conducted, each lasting 30 s. Imaging parameters were: $\alpha = 25°$, $N_{echoes} = 8$, $\Delta TE = 12$ ms, TR = 110 ms, matrix = 256^2, FOV = 192 mm, slice thickness = 8 mm.
Results: Thirteen of fourteen patients (13m, 1f) with 16 lesions were studied successfully. MRI measurements were obtained from primary tumor (PT) alone in 7/13 patients, from PT and lymphatic node (LN) in 3/13 patients and from LN alone in 3/13 patients.
Marked interindividual tumor tissue oxygenation changes while breathing carbogen or O_2 were seen. Pixel by pixel analysis of the T2* values showed a shift towards higher values corresponding to an oxygenation increase in most but not all patients. However, a considerable intratumoral heterogeneity was also observed.
Conclusions: Detection of oxygenation changes in head and neck tumor patients is feasible by the presented MRI technique. It may be used for monitoring individual tissue response to hyperoxia and help preselect patients for individual treatments using hyperoxic gas mixtures.

1102 ORAL

Improved delineation of lymph node basins at risk in pelvic malignancies using magnetic resonance lymphography with ferumoxtran-10 for radiotherapy treatment planning

R. Dinniwell, P. Chan, M. Haider, A. Fyles, A. Syed, A. Kirilova, G. Czarnota, D. Jaffray, M. Milosevic. *Princess Margaret Hospital, Radiation Oncology, Toronto, Canada*

Purpose: To determine the utility of Magnetic Resonance Imaging (MRI) with an ultra-small superparamagnetic iron oxide that delineates phagocytotic activity within lymph nodes as a means of lymph node target definition to generate a nodal clinical target volume comprised of the nodal basins at risk of tumor spread.
Methods: All patients with histologically confirmed prostate, bladder, cervical or endometrial cancer were eligible for this prospective trial. Each patient underwent pre- and post-contrast MRI studies over two consecutive days. Axial images were obtained at 3 mm intervals through the pelvis. Ferumoxtran-10 (Combidex®: Advanced Magnetics, Inc, Cambridge, MA) was administered on the first day immediately after the initial MRI. The pelvic vasculature and lymph nodes were delineated from the origin of the inferior mesenteric artery to the ischial tuberosities using 3D modeling and image processing software (3D-DOCTOR®: Able Software Corp., Lexington, MA). Lymph node frequency and location relative to the adjacent vascular segments was analyzed using Matlab (MathWorks Inc., Natick, MA). Each lymph node was divided into $0.5 \times 0.5 \times 3$ mm^3 nodal voxels. The minimal distance between the centre of each nodal voxel and the closest artery or vein (in three-dimensions) was calculated for each of the vascular segments.
Results: 50 patients were enrolled (32 prostate; 8 bladder; 5 cervical and 5 endometrial carcinomas). Preliminary analysis reveals the maximum distance of the lateral most aspect of the lymph nodes from the closest vessel (either artery or vein) to be between 2.5 and 32 mm (mean 7.5). Analysis by vascular segment revealed the distances between the nodal voxels (percent of total nodal volume) and the closest vessel edge (mm) to be: distal Para-Aortic Artery and Inferior Vena Cava: 50%-4.69; 90%-10.55; 95%-11.63; Common Iliac Artery and Vein: 50%-4.04; 90%-8.17; 95%-8.76; and Internal and External Iliac Artery and Vein: 50%-6.65; 90%-14.27; 95%-17.51. Radial expansion around the major pelvic vessels failed to adequately encompass all of the lymph nodes at risk.
Conclusion: The use of MRI lymphography with ferumoxtran-10 enables the visualization of pertinent lymph node locations in a three-dimensional projection. This imaging technique may improve IMRT treatment planning by identifying those lymph nodes at risk of harbouring occult metastatic disease.