from 15.4 to 27.3 per minute. Rotations, respiratory amplitudes and frequencies showed significant interindividual differences ($p < 0.0001$). We found no correlation between age, body-mass-index and surgical status, and uncertainties from positioning and patient movement.
Conclusions: Positioning accuracy and respiration-dependent motion vary significantly between individual patients. Considering characteristic patient-dependent motion patterns and taking into account also potential time-dependent changes, individually tailored radiotherapy planning and delivery should be the subject of further investigations.

1373 POSTER

Postoperative radiation therapy for pituitary adenomas: analysis of tumour control and hormonal sequelae

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Background: The role of postoperative radiotherapy in the management of pituitary adenomas is still controversial. The aim of our study was to evaluate local tumour control and the incidence of hypopituitarism following pituitary surgery and radiotherapy.
Patients and methods: Between 4/1984 and 11/1991, 89 patients (43 female, 46 male) with pituitary macroadenomas received external beam radiotherapy at the Department of Radiation Oncology, Graz, Austria. Prior to radiotherapy all patients had undergone surgery (transsphenoidal, n = 86, craniotomy, n = 3), six patients had undergone two or more previous tumour resections. Fifty-five patients had functional and 34 patients had non-functional adenomas. Fifteen patients received radiotherapy after complete tumour resection and 74 patients for residual disease. Radiotherapy was delivered in a three field technique and a mean total dose of 50.2 Gy (range 23.4 – 54 Gy).
Results: Pituitary tumour regrowth has occurred in 6 of the 89 patients (6.7%) during a mean follow up of 76 months (range, 1.5 to 166 months). Three of these patients required a second surgical procedure. In 73 patients information on hormonal function was available and in 65 of them (89%), hormonal insufficiency was observed (partial hypopituitarism, n = 61, panhypopituitarism, n = 4). Forty five patients (62%) developed a deterioration that required hormonal replacement therapy.
Conclusions: Radiotherapy after pituitary surgery is highly effective in preventing recurrence of pituitary adenomas. Multiple endocrine axes, however, were commonly involved with an overall frequency of 89% and therefore patients need lifelong endocrine follow up after combined treatment of the pituitary region.

1374 POSTER

Modulation of radiation response by histone deacetylase inhibition

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Background: Histone deacetylase (HDAC) inhibitors, which modulate chromatin structure and gene expression, represent a class of anticancer agents that hold particular potential as radiation sensitizers. In this study, we examine the capacity of the HDAC inhibitor suberoylanilide hydroxamic acid (SAHA) to modulate radiation response in human tumor cell lines and explore potential mechanisms underlying these interactions.
Materials and methods: Exponentially growing tumor cells were incubated in medium containing 0–10 μM of SAHA for 92 h. Cells were fixed with crystal violet to estimate cell viability. Caspase activity was analyzed by fluorescence spectroscopy using a fluorescein labeled pan-caspase inhibitor. Cells were harvested after 72 h of exposure to SAHA (1.0 μM), radiation (7 Gy), or the combination. Whole cell lysates were evaluated for poly(ADP-ribose) polymerase (PARP) cleavage by western blot analysis. Cells were exposed to varying doses of radiation ±5 days pretreatment with SAHA (0.75–1.0 μM). After incubation intervals of 14–21 days. Cells were grown and treated in chamber slides. At specified times after treatment with SAHA, cells were fixed in paraformaldehyde, permeabilized in methanol, and probed with primary and secondary antibody solutions. Slides were analyzed using an epifluorescent microscope.
Results: SAHA induced a dose-dependent inhibition of proliferation in human prostate and glioma cancer cell lines. Exposure to SAHA enhanced radiation-induced apoptosis as measured by caspase activity ($p < 0.01$) and PARP cleavage. The impact of SAHA on radiation response was further characterized using clonogenic survival analysis, which demonstrated that treatment with SAHA reduced tumor survival after radiation exposure. We identified several oncoproteins proteins that show differential expression after exposure to SAHA. These proteins may contribute to mechanistic synergy between HDAC inhibition and radiation response.
Conclusion: These preclinical results suggest that treatment with the HDAC inhibitor SAHA can enhance radiation-induced cytotoxicity in human prostate and glioma cells. We are examining the capacity of HDAC inhibitors to modulate radiation response and tumor control in animal xenograft model systems to strengthen the rationale for future clinical trial exploration.

1375 POSTER

Differential effects of polyunsaturated fatty acids on the radiosensitivity of normal colorectal and colorectal adenocarcinoma cell lines

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Background: Animal and in vitro studies have demonstrated that n-3 polyunsaturated fatty acids (PUFAs) are cytotoxic against a variety of malignant cells including colonic adenocarcinoma. However the effect of PUFAs on normal colorectal epithelial cells has not been established. The aim of our study was to investigate the effect of n-3 and n-6 PUFAs on a normal colon and 2 colonic adenocarcinoma cell lines. We also evaluated the effect of PUFAs on the radiosensitivity of these cell lines.
Method: The 2 colon adnenocarcinoma cell lines (SW480, SW620) and normal colon (CRL7418) cell line were incubated with n-6 PUFAs: arachidonic acid (AA), linoleic Acid (LA) and n-3 PUFAs: Alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) with or without radiation (0–5 Gy). Radiation cell survival was assessed with trypan blue exclusion assay and MTT assay. Annexin-V staining for apoptosis and flow cytometry were used to evaluate the mechanism of PUFAs and radiation interaction.
Results: The 3 cell lines were incubated with various concentration (0, 50, 100 and 200 μM) of PUFAs for 4 days for cytotoxicity assay. LA, ALA, EPA and DHA inhibited SW480 and SW620 cell growth in a dose-dependent manner. In contrast, low doses (<100 μM) of PUFAs enhanced the proliferation of CRL7418 cells. Preincubation of the 2 cancer cell lines with DHA (50 μM) for 24 hrs prior to radiation resulted in an enhanced radiation cell kill. Interestingly, 50 μM DHA protected the CRL7418 cells from radiation damage. ANNEXIN-V staining showed that DHA induced apoptosis in both cancer and normal cells. All of the PUFAs did not have any effect on the cell cycle progress.
Conclusions: In conclusion, we have demonstrated that PUFAs are cytotoxic to colorectal cancer cells and DHA can act as a radiosensitizer. In contrast, PUFAs have no cytotoxic effect on normal colorectal cells and in fact can act as a radioprotector. The results provide in vitro rationale for the use of n-3 PUFAs in combination with radiation therapy for the treatment of colorectal cancer.

1376 POSTER

Clinical results of intracoronary radiotherapy for In Stent Restenosis (ISR)

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Background: Treatment of in-stent restenosis with PTCA alone is considered to be relatively ineffective. Mechanisms of repair result in intimal hyperplasia followed by early re-restenosis. There is evidence that ICBT can reduce the probability of a in-stent restenosis after PTCA due to inhibition of neointimal formation within the stent.
Patients and methods: 40 Pat. (27 m., 13 f, age: 66.9 years) were retrospectively analysed. All patients were treated by using the Novoste-Beta-CathTM-3,5F System after PTCA. The target vessel received 18.4 to 25.3 Gy of radiation at a depth of 2 mm from the center of the source as recommended by the Novoste company. Times of ISR before and after ICBT were registered and restenosis free survival and overall survival were calculated by Kaplan-Meier-Analysis (log-rank). The time interval between last PTCA without ICBT and the consecutive recurrence was compared with the follow up time after PTCA with ICBT.
Results: The three year overall survival rate after ICBT was 93%. The 1/2, 1, 2 and 3 year ISR-free survival rate after PTCA + ICBT were 81, 72, 52 and 38%, respectively. After PTCA alone the 1/2, 1 and 2 year ISR-free survival rate was 30, 13 and 0%. This difference was highly significant ($p < 0.0001$). Patients with more than two IRS before ICBT had a better outcome (3 year IRS-free survival: 80%) than patients with only one or two IRS before ICBT (25%, $p < 0.05$).

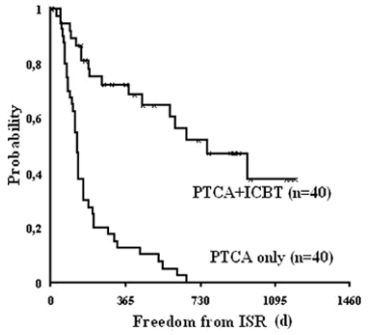

Fig. 1

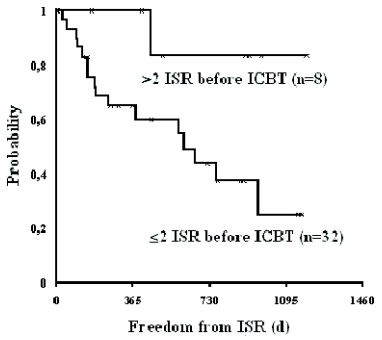

Fig. 2

Conclusion: ICBT is highly effective and save in patients with ISR. Our results are in accordance to the WRIST and BETA-WRIST data that showed an ISR-free-survival-rate of 86% after 1/2 year (WRIST) and 66% (BETA-WRIST). The ISR-rates in our control group (70%) were comparable to the placebo-groups in WRIST (68%) and BETA-WRIST (72%). However, in our study the follow up was longer than in the randomised trials. After 3 years only 38% of the patients were without IRS. Surprisingly, patients with >2 ISR before ICBT had the lowest ISR-rate after ICBT.

1377 POSTER

Movement of the cervix in after-loading brachytherapy: implications for designing external beam radiotherapy boost fields

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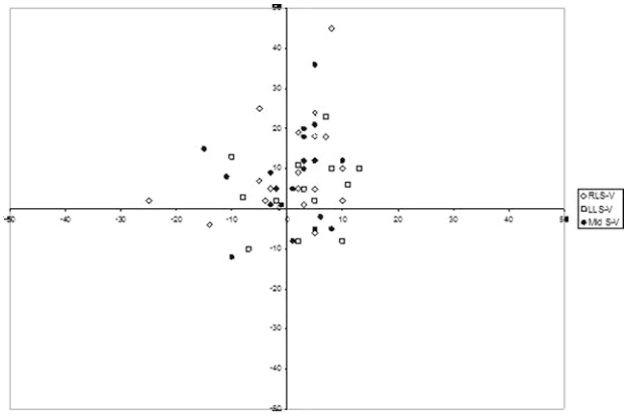
Background: Patients with invasive carcinoma cervix treated by chemoradiotherapy and brachytherapy may also receive pelvic side wall boost using a midline shield (MLS). The purpose of this study is to assess the usefulness of implanted gold grains in detecting the movement of the cervix caused by the insertion of low dose rate brachytherapy applicators and its implication in designing MLS.
Materials and methods: The medical records of 42 patients with various stages of cervical carcinoma, who were treated by radical chemoradiotherapy from August 1999 to December 2003, were reviewed. All of these patients underwent examination under general anaesthesia and gold grain insertion to demarcate the vaginal tumour extent, in the anteroposterior and lateral planes, prior to the start of external beam RT. The isocentric orthogonal films (simulator films) of external RT and brachytherapy were compared to asses the change in position of the gold grains and the consequences for the design of the MLS for parametrial and pelvic side wall boost.
Results: A significant shift in the position of the gold grains was noted in both the *x* (lateral) and the *y* (cranial/caudal) axes, ranging from 1 mm to 46 mm. The median shift of midline, right and left lateral gold grains was 4.5, 5 and 7 mm in the *x*-axis while it was 10, 8, and 9.5 mm in the *y*-axis. The majority of gold grains were shifted both cranially (80%) and laterally (69%). Thirty two patients received parametrial boost RT of which 25(59.3%) patients had a customised, pear-shaped shield and the remaining 7(16.6%) had a straight sided, rectangular MLS. Four patients relapsed locally and 3 of these had been treated using a customised shield. In 2 of these 4 patients, there was an absolute under-dosage of the central pelvis at the tip of the intra-uterine tube, by 50% of the parametrial boost dose (5.4 Gy/3#/3days).



Scatter diagram showing the shift of gold grains in both the *x* and *y*-axes. Lateral shift in the *x*-axis and cranial shift in the *y*-axis are given positive signs. (RLS-V: Right lateral, LLS-V: Left lateral, Mid S-V: Midline gold grains)

Conclusions: The after loading brachytherapy in the management of carcinoma cervix results in significant shift of cervix and under-dosage of the central pelvis while delivering parametrial boost radiotherapy. Although this did not result in a statistically significant local relapse rate, the resulting under-dosage can be avoided by designing customised MLS taking account of the shift in the gold grain markers and potentially improving local control of disease.

1378 POSTER

Dosimetric correlations with radiation esophagitis in intrathoracic malignancy

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Background: Acute radiation esophagitis was assessed according to clinical and dosimetric parameters in patients treated with thoracic radiotherapy (TRT).
Material and methods: Subjects comprised 61 patients who received TRT for lung cancer (n = 43, 70%) or mediastinal malignancies (n = 18, 30%) between February 2000 and April 2005. Median age of patients was 68 years (range, 26–88 years). Underlying pathology was non-small-cell lung cancer (n = 34, 55%), small-cell lung cancer (n = 9, 15%), thymoma (n = 4, 7%), thymic cancer (n = 7, 11%), malignant lymphoma (n = 2, 3%), mediastinal seminoma (n = 1, 2%), mediastinal liposarcoma (n = 1, 2%), or other mediastinal malignancy (n = 3, 5%). A median dose of 60 Gy (range, 40–66.6 Gy) was administered to the isocenter in single daily fractions of 1.8 or 2 Gy. With heterogeneity corrections, median dose administered to the isocenter was 60.0 Gy (range, 39.7–68.2 Gy). A total of 41 patients (67%) were treated with concurrent chemoradiotherapy comprising platinum agent (cisplatin or carboplatin) combined with: paclitaxel (n = 24, 39%); irinotecan hydrochloride (n = 7, 11%); vincristine sulfate and etoposide (n = 2, 3%); vinorelbine ditartrate (n = 1, 2%); etoposide (n = 4, 6%); doxorubicin hydrochloride, cyclophosphamide and etoposide (n = 1, 2%); vindesine sulfate and mitomycin C (n = 1, 2%); or docetaxel (n = 1, 2%). Esophageal toxicities were graded according to Radiation Therapy Oncology Group criteria. The following factors were analyzed with respect to associations with Grade 1 or worse esophagitis using univariate and multivariate analyses: age; gender; concurrent chemotherapy; chemotherapeutic agents; overall duration of TRT; maximal esophageal dose; mean esophageal dose (D mean); and percentage of esophageal volume receiving >10 Gy (V10) to >65 Gy (V65) in 5 Gy increments.
Results: A total of 43 patients (70%) developed acute esophagitis: Grade 1, n = 36 (59%); or Grade 2, n = 7 (11%). No patients displayed acute esophageal toxicity of Grade 3 or worse. Univariate analysis revealed significant associations with esophagitis for D mean ($p = 0.007$), V10-V55 ($p<0.05$) and chemotherapeutic agents ($p = 0.015$). The most significant correlation was between esophagitis and V35 on univariate ($p = 0.001$) and multivariate analyses ($p = 0.020$).
Conclusions: V35 was the most significant factor associated with mild acute esophagitis.