acquisition technique can give a wide cranio-caudal coverage beyond the detector width for the same respiratory phase; however, motion artifacts are not mitigated completely due to the low temporal resolution. Therefore, uncertainties of the actual position, volume, and shape of a moving object result in planning errors in radiotherapy treatment planning CT. Respiratory motions during irradiation may cause the radiation beam to miss a portion of the target volume.
Conclusions: The RS-FDK has capabilities for high temporal resolution and good SNR. Therefore, we expect it will demonstrate good ability to significantly increase accuracy in the dose distribution. It will be useful for more precise treatment planning for respiratory-moving tumors. We have already found that it is possible to achieve more precise radiotherapy including 4D radiation therapy with the RS-FDK.

1370 POSTER

Microbeam Radiation Therapy (MRT) applied to rats' brain tumor: finding the best compromise between normal tissue sparing and tumor curing

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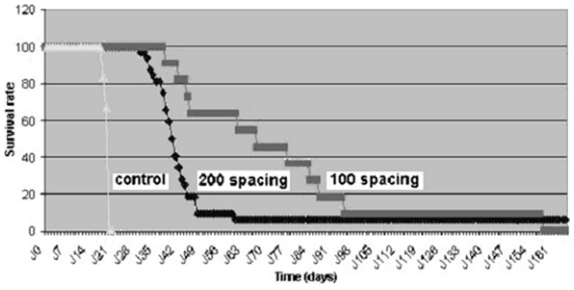
Microbeam Radiation Therapy (MRT) (Laissue et al; 1998; Int J Cancer) consists of irradiating animals with very high doses (>100 Gy) delivered by arrays of microbeams (MB), which are few micrometers wide and few hundreds of micrometers spaced. This preclinical therapy is presently applied in synchrotron radiation sources where high intense, quasi parallel X-ray microbeams can be produced. MRT is based on the dose/volume effect, and literature reports cases of brain tumors cured in rats by MRT while sparing the surrounding normal tissues. Irradiation parameters are various and include the skin dose, the dose rate, the X-ray beam spectrum, the width and the spacing between the MB.
10^4 9L gliosarcoma cells contained in 1 μl were stereotactically implanted in the right caudate nucleus of Fisher rats at day 0. Between day 11 and 13, an MRI examination was performed to confirm the presence of tumors. At day 14, tumors were laterally irradiated either from right hemisphere to left hemisphere or from left hemisphere to right hemisphere by using 50 MB covering a $10.5 \times 12\ mm^2$ field. After irradiation, rats were weighted 3 times per week, and clinical signs were annotated. At the death/euthanasia of rats, brains were taken for histology. Experiments were performed using a skin entrance dose of 625 Gy, MB of 25 μm in width, and spacing of 200 or 100 μm.
Rats irradiated with 200 μm spacing showed normal weight curves after implantation with a decrease before death, which occurred at 41.6 days (left to right) and 37.9 days (right to left) in average after the implantation. All rats were found with a brain tumor, except 2 rats (1 for each irradiation direction) that were cured (and survived more than 600 days). Very few of those rats present clinical signs after irradiation (4/32). On the contrary, rats irradiated with 100 μm spacing showed unusual weight curves, always below 300 g, in parallel with neurological disorders (8/11). Average lifespan was 64.2 days after tumor implantation with a long term survivor (154 days). Four of those rats presented no brain tumors at the histological examination.



Survival curve of series at 200 spacing, 100 spacing and control

Results suggest that this technique can ablate only few tumors at 200 μm spacing while preserving the normal tissue. The 100 μm spacing appeared too aggressive for the normal tissues, even if tumors can be ablated more efficiently. Future experiments will aim at performing a fine tuning of irradiation parameters to find the adequate balance between 100 and 200 μm spacing.

1371 POSTER

Comparison of locoregional recurrences following postmastectomy radiotherapy using electrons or photons: poor supraclavicular node control of electron beam irradiation in patients with four or more positive axillary nodes

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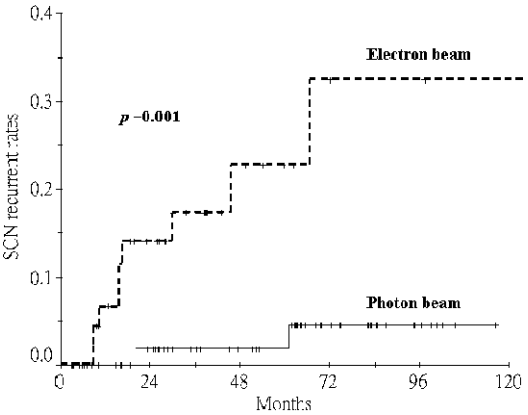
Background: We retrospectively compared locoregional (LR) recurrence between electrons and photons for postmastectomy radiotherapy.
Materials and methods: From January 1988 to December 1999, 124 and 122 women with breast cancer of AJCC 2002 stage II and III received electrons and photons irradiation following modified radical mastectomy, respectively. Doses of 46–52.2 Gy/23–29 fractions were delivered to the chest wall (CW) and peripheral lymphatic drainage with 12–15 MeV single-portal electrons or 6 MV photons. Eighty-four patients received an additional 6–20 Gy boost to the surgical scar using 9 MeV electrons.
Results: The 8-year rates of LR recurrence were 19% and 10% ($p = 0.071$) in patients receiving electrons and photons, respectively. The corresponding rates of CW recurrence were 12% and 7% ($p = 0.227$). However, recurrent rate of ipsilateral supraclavicular node (SCN) was significantly higher in patients following electrons (11%) than photons (3%) irradiation ($p = 0.025$). In multivariate analysis of CW recurrence, N2–3 stage (positive axillary nodes $\geqslant 4$) ($p = 0.013$) and diabetes ($p = 0.004$) were independent factors. Multivariate analysis of ipsilateral SCN recurrence revealed interaction between N2–3 stage and electrons ($p<0.001$). The interaction was also noted for LR recurrence ($p<0.001$). Further subgroup analyses revealed the beneficial effect of photons existed only in N2–3 stage for SCN ($p = 0.008$) and LR ($p = 0.006$) recurrence but not N0–1 stages.



Conclusion: Photons may be superior to electrons for treatment of N2–3 breast cancer. The impact of electrons on LR control may result from poor SCN control. A single-portal electron is not suggested for these patients.

1372 POSTER

Interindividual variations in positioning accuracy and patient motion during pelvic radiotherapy

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Purpose: Safety margins are in general based on population-averaged measurements. The aim of this study is to investigate interindividual differences in positioning accuracy and motion characteristics as a basis for individualized treatment planning.
Materials and methods: For 10 patients with gynecological carcinomas positioning accuracy was evaluated using repeated electronic portal images. Inter- and intrafractional patient movement was registered by online documentation of body marker movement using the ExacTrac system (Brainlab, Munich, Germany). From these data, values for individual random and systematic positioning errors in all directions including rotational angles were calculated. Further, patient-dependent movement during radiotherapy was analyzed including respiratory amplitudes, mean breathing positions and respiratory frequencies. Patient-specific clinical parameters were correlated with positioning and motion data.
Results: Individual systematic positioning errors ranged from −7.4 to 10.4 mm for the three coordinates ($p < 0.0001$), individual random positioning errors from 1.6 to 4.8 mm ($p > 0.05$). Mean rotation errors were between −0.7 and 2.3 degrees. Over the radiation series individual mean respiratory amplitudes ranged from 0.7 to 5.2 mm, mean frequencies

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%, $p < 0.05$).