and antineoplastic properties. The aim of this study was to evaluate radioprotective effect of RGZ on a murine model of late pulmonary damage and of acute intestinal damage.
Materials and Methods: *Lung fibrosis*: C57BL/6 mice were treated with the radiomimetic agent bleomycin 40 mg/kg every 2 days for 5 administrations, with or without RGZ(5 mg/kg/day) started 24h before bleomycin treatment. To obtain an independent qualitative and quantitative measure for lung fibrosis we used high resolution CT, performed twice a week during the entire observation period. Hounsfield Units (HU) of section slides from the upper and lower lung region were determined. On day 31 mice were sacrificed and lungs collected for histopathological analysis.
Acute intestinal damage: mice underwent 12 Gy total body irradiation (TBI) with or without RGZ(5 mg/kg/day) started 24h before TBI. Mice were sacrificed 24 or 72h after TBI and ileum and colon segments were collected for histopathological analysis.
Results: *Lung fibrosis:*starting from 10th day of bleomycin treatment, mice showed typical CT features of lung fibrosis including irregular septal thickening, and patchy peripheral reticular abnormalities with intralobular linear opacities, Accordingly HU lung density was dramatically increased. RGZ markedly attenuated the radiological signs of fibrosis and strongly inhibited HU lung density increase (60% inhibition at the end of the observation period). Histological analysis revealed that in bleomycin-treated mice fibrosis involved 50−55% of pulmonary parenchyma and caused an alteration of the alveolar structures in 10% of parenchyma, while in RGZ-treated mice fibrosis involved only 20−25% of pulmonary parenchyma without alterations of the alveolar structures.
Acute intestinal damage: 24h after 12 Gy TBI intestinal mucosa showed villi shortening, mucosal thickness and crypt necrotic changes; chorion showed oedema and inflammatory infiltrate. RGZ showed an histological improvement of tissue structure, with villi and crypts normalization and oedema reduction.
Conclusions: These results demonstrate that RGZ displays a protective effect on pulmonary fibrosis and radiation-induced intestinal toxicity in mice, and although further investigations are necessary, it could be proposed as radioprotective agent.

2005 ORAL

Dose per Pulse Is a Relevant Factor That Impacts Radiation Response on Two Glioblastoma Cancer Cell Lines

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Background: The question to what extent delivery time or dose rate impact tumour cell survival has a long history in radiation therapy. While there is increasing evidence in the recent literature that extended delivery time might impact cancer cell survival, we are short of studies investigating the potential effect of modified dose rate on cancer cells, mostly due to technical challenges.
Material and Methods: To perform our experiments, we used the TrueBeam STx linear accelerator (Varian Medical Systems, Palo Alto, CA, USA), which allows generating a pulsed photon beam of the nominal energy of 10 MV with the flattening filter in place (X10) as well as flattening filter-free, referred to as X10 and X10 FFF, respectively. Removing of the flattening filter leads to a decrease of the beam's mean energy and to an increase of dose delivered per pulse (DPP) of radiation. To validate the radiobiological effect of these two beams on cancer cells, we treated two glioblastoma cell lines, T98G and U87-MG, with either 5 or 10 Gy single dosage using different dose rates (with flattening filter: 20 and 400 MU/min; without flattening filter: 400 and 2400 MU/min) and tested their potential effect on cancer cell survival with the colony formation assay. To better understand the molecular mechanism we performed microarray chip analysis.
Results: In our experimental setting dose delivered per pulse seemed to be a crucial factor that influences cancer cell survival. Comparing the effect on cancer cells of the radiation with 400 MU/min using X10 to 400 MU/min using X10 FFF, the X10 FFF beam was more efficient in reducing cancer cell survival than the X10. Throughout this treatment, delivery time was kept the same while dose per pulse was significantly higher in the treatment using X10 FFF. This effect became more relevant the higher the single dose. In addition, treatment with X10 FFF comparing 400 MU/min to 2400 MU/min did not show any significant difference. In this experiment, delivery time was significantly faster using 2400 MU/min, while the dose per pulse was kept the same.
Conclusions: The results presented here show that dose per pulse might become a crucial factor which influences cancer cell survival. Understanding the mechanisms by which dose rate and dose per pulse influence cancer cell survival might lead to new approaches for the therapy of treatment-resistant tumours and is currently a topic of investigation in our laboratory.

2006 ORAL

Novel Technology of Laser Driven Proton Beams for a Potential Application in Cancer Therapy: in Vitro Dose Response Studies

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Background: The development of the new technology of proton and ion acceleration by ultra-high intensity lasers for cancer therapy is the goal of the German joint research project "onCOOPtics". The laser based acceleration promises compact and economic therapy facilities that are suitable for already existing clinics. In contrast to conventional particle acceleration the laser based method results in beams of very short pulses with ultra-high pulse dose and correspondingly peak dose rate. Within the project multidisciplinary issues like development and optimization of high-intensity laser systems, efficient proton acceleration schemes and proton beam transport are handled. Moreover, the physical and real-time dosimetric characterization as well as the investigation of radiobiological consequences of laser accelerated beams are essential. These imply translational investigations starting from *in vitro* cell irradiation.
Material and Methods: Systematic *in vitro* cell experiments were performed at the 150 terawatt laser facility DRACO at HZDR. Proton pulses up to 20 MeV were accelerated, whereas the broad proton spectrum was downward limited to 6 MeV using an energy-filter-system. An in-house developed integrated dosimetry and cell irradiation system (IDOCIS) was tested and calibrated allowing precise dosimetry as well as the exact positioning of each cell sample. Cell survival and residual DNA double strand breaks were determined after irradiation of the tumour cell line SKX in a dose range from 0.5 Gy to 4.3 Gy. Additionally, reference irradiation were performed with continuous proton beam at a conventional Tandem accelerator and with a 200 kVp X-ray tube.
Results: A stable and reproducible laser driven proton beam was achieved for experiments over weeks including real-time dose and energy spectrum monitoring as well as precise absolute dosimetry. The comparison of the radiobiological effectiveness of conventional and laser accelerated proton beams show no significant difference for *in vitro* cell irradiation.
Conclusions: These first systematic *in vitro* cell response studies with precise dosimetry of laser driven protons represent an important step toward the development of laser accelerated particles for radiotherapeutic application. Further experiments with other human cell lines and *in vivo* studies are under way.
The work was supported by the BMBF, grant no. 03ZIK445.

Poster Presentations (Mon, 26 Sep, 09:30−12:00) **Radiobiology/Radiation Physics/Radiotherapy**

2007 POSTER

Study on Liver Cancer Target Volume Variations Between 4D-CT and 3D-CT Associated With Active Breathing Control Device

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Background: The study aimed to observe and analyze the variations of liver cancer GTV between 4D-CT and 3D-CT associated with active breathing control device (ABC).
Methods: 13 cases with primary liver cancer were selected and underwent CT simulation and localization. Each case underwent 4D-CT scanning first, with ABC device working on to monitor and analyzes the breath wave. Afterwards, 3D-CT scanning were underwent, respectively when patient breathing freely, at the end of inspiration and expiration. GTVs were contoured, according the same criterion by one radiologist and one radiation oncologist jointly, respectively on 6 CT series: CT0 series (4D-CT end-exhale), CT50 series (4D-CT end-inhale), 4D-CT MIP series, 3D-CT free breathing CT series, 3D-CT end-exhale series, and 3D-CT end-inhale series, which were named GTV4D-0, GTV4D-50, GTVMIP, GTVFB, GTVEE, GTVEI. Afterwards, GTV4D-M were obtained by merging GTV4D-0 and GTV4D-50, meanwhile GTV3D-M were obtained by merging GTVEE and GTVEI. The volume of all GTVs were measured and analyzed using SPSS software. Paired Wilcoxson test was applied.
Results: There was no significant difference between GTVEI and GTVEE ($P = 0.325$), as well as GTVEI and GTV4D-0 ($P = 0.125$), GTVEE and GTV4D-50 ($P = 0.325$), GTV4D-0 and GTV4D-50 ($P = 0.125$), GTV4D-M

and GTV3D-M (P = 0.125), GTVMIP and GTV3D-M (P = 0.325). GTVFB was smaller than GTV3D-M and GTV4D-M significantly (P = 0.015 and P = 0.016), and than GTVMIP without significant difference (P = 0.125). Notably, GTV4D-M differed from GTVMIP (P = 0.016).
Conclusions: The margins from GTV to PTV should be noticed, when undergo CT simulation with patients breathing freely, due to the differences between GTVFB and GTV4D-M and GTV3D-M. To merge GTVEE and GTVEI could be an alternative to using 4D-CT for simulation.

2008 POSTER

Assessment of Anatomical and Dosimetric Changes by a Deformable Registration Method During the Course of Intensity-modulated Radiotherapy for Nasopharyngeal Carcinoma

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Background: To quantify the anatomic variations and the actual dosimetric effects by a deformable registration method throughout the entire course of simultaneous integrated boost intensity-modulated radiotherapy (SIB-IMRT) and to assess the necessity of re-planning for patients with nasopharyngeal carcinoma (NPC).
Methods and Materials: Twelve patients with locally advanced NPC treated with SIB-IMRT were enrolled in this pilot study. Plan1 (CT1) was based on the original CT scan, while Plan2 (CT2) was generated from the mid-treatment CT scan (CT2), which was acquired after 20−25 fractions of IMRT of Plan1. All plans were calculated with an inverse planning system (Pinnacle3, Philips Medical System). Both sets of CTs, RTstructures and RTdoses for the two plans were transferred to MIMsoftware (V5.1) workstation, and then hybrid IMRT plan, Plan1 (CT2), was generated by deforming doses of Plan1 to CT2 allowing for visualizing the dose that had been delivered on the current anatomy. In additional, the accumulated plan, Plan1+2 (CT2), was generated to quantify the actual dosimetric effects during the course of treatment. The dose-volume histogram of actual and hybrid plans were compared.
Results: Compared to CT_1, the volume of the right and left parotid glands decreased by 24.6±11.9% and 35.1±20.1%, and planning target volumes of the gross target volume (PGTV), the regions at high risk for microscopic disease (PTV_2) and low risk elective nodal coverage (PTV_3) reduced by 16.4±27.3%, 3.8±6.3% and 8.8±12.0% in CT_2. In $Plan_1$ (CT_2) and $Plan_{1+2}$ (CT_2), the dose to 95% of PGTV decreased by 3.9±2.5% and 1.7±1.8%, the maximum dose (D_{max}) to the spinal cord increased by 3.8±5.3% and 0.5±1.9%, and increased by 0.8±4.4% and 1.2±3.3% to brainstem compared to $Plan_1$ (CT_1), respectively. The mean dose (D_{mean}) to the left parotid gland increased by 4.4±20.4% and 2.0±15.0% in $Plan_1$ (CT_2)and $Plan_{1+2}$ (CT_2), while D_{mean} to the right parotid gland increased by 0.2±7.9% in $Plan_1$ (CT_2) and reduced by 1.1±8.7% in $Plan_{1+2}$ (CT_2). Our data demonstrated that without repeat imaging and replanning during the course of IMRT, the dose to target reduced and the dose to critical structures increased.
Conclusions: During the course of IMRT for patients with NPC, the volumes of targets and parotid glands reduced significantly. Mid-treatment CT scanning and replanning were recommend to ensure adequate doses to the targets and safe doses to the critical normal tissues.

2009 POSTER

Do Obesity and Set-up Position Affect the Interfractional Variation of Pelvic Irradiation?

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Background: Our aim is to examine the relation of obesity and set-up position with the set-up error in large sized population with conventional fractionated pelvic irradiation with a modern verification technique.
Material and Methods: Consecutive 101 patients with whole pelvic irradiation were analyzed with a prospective manner. Daily verification using a kilo-voltage orthogonal on-board imager was performed. The set-up errors between two origins (isocenter of simulation ($\Delta Shift^{Sim}$) and the initial treatment ($\Delta Shift^{Ini}$) and each fraction were measured as to the systematic shifts along right-to-left (RL), superior-to-inferior (SI), and anterior-to-posterior (AP) axes and 3 dimensional (3D) vectors. The estimation was based on measurements in a population of patients. The overall mean error, M, the standard deviation (SD) of the systematic error, Σ, and the SD of the random error, σ were determined. Set-up position was divided into supine (N = 53) and prone (N = 47). Body mass index (kg/m^2) was classified in four groups [underweight <18.5 (N = 6), normal <25 (N = 56), overweight <29.5 (N = 34), obese >29.5 (N = 5)]. A T-, Tukey-b and F-test for the comparison of two Ms, multiple Ms and SDs were used, respectively. A p value <0.05 was significant.
Results: In $\Delta Shift^{Sim}$, the M of 3D vector was 6.19 and 5.49 mm for supine and prone, respectively ($p = 0.237$). None of the difference of Σ along any axis was observed. While σ along RL was better in prone (p = 0.001), AP was better in supine ($p = 0.008$). In $\Delta Shift^{Ini}$, the M of 3D vector was 3.02 and 3.64 mm for supine and prone, respectively ($p = 0.073$). The Σ along AP was better in supine ($p = 0.044$) In terms of σ, similar tendency was observed (RL, $p = 0.001$; AP, $p = 0.002$). The M of 3D vector of $\Delta Shift^{Sim}$ was 4.37, 5.52, 6.08, and 10.16 mm for underweight, normal, over-weight and obese, respectively ($p = 0.003$) The Σ along RL in obese was more extensive than others ($p < 0.000$). The Σ along other axes in obese was worse than others without significance (SI, $p = 0.081$; AP, $p = 0.070$). In $\Delta Shift^{Ini}$, the range of M of 3D vector was from 2.91 to 4.13 mm ($p = 0.591$). The σ along RL in obese was more extensive than others in both $\Delta Shift^{Sim}$ ($p < 0.000$) and $\Delta Shift^{Ini}$ ($p < 0.000$).
Conclusions: The effect of set-up position to the set-up error is inconsistent along all directions and insignificant. Obesity is a risk factor of extensive set-up errors. However, some of set-up errors could be properly corrected with initial on-board imager verification.

2010 POSTER

Genetic Hypersensitivity to Ionizing Radiation

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Background: Exposure to medical radiation has increased over time. Radiotherapy has a crucial role in management of cancers. Hypersensitivity to ionizing radiation has been observed in some genetic syndromes.

Table: Radiosensitive phenotypes

Human disorder	Major clinical features	Cancer type	Frequency	Gene	Pro obs	Is gene-radiation interaction definitive?
Ataxia telangiectasia	Cerebellar ataxia, immuno-deficiency, oculocu-taneous telangiectasia	Lymphoma, leukaemia, epithelial carcinomas	1:300,000	*ATM*	Avoiding mammography/ CT. Reduced dosage/duration of RT if not avoidable	Yes
Fanconi anaemia	Bone marrow deficiency, short stature, intellectual deficiency, radial hypoplasia	Leukaemia, squamous cell carcinoma of oropharynx, oesophagus, vulva	3:1,000,000	*FANCA, FANCC, FANCG*	Reduced dosage/duration of RT if not avoidable	Yes
Gorlin syndrome	Odontogenic jaw keratocysts, palmar/ plantar pits, skeletal abnormalities	Basal cell carcinoma, medullo-blastoma	1:40,000	*PTCH*	RT induces basal cell carcinoma development	Yes
Ligase IV syndrome	Growth deficiency, skin photo-sensitivity developmen-tal delay, immuno-deficiency	Leukaemia, multiple myeloma, lymphoma	Very rare	*LIG4*	Avoiding RT	Yes
Li-Fraumeni syndrome		Breast carcinoma, sarcoma, leukaemia, brain tumour	Very rare	*TP53*	Mammography/ MRI for breast screening. Minimizing dosage/duration of RT	RT induced cancer observed but gene-radiation interaction not found
Neuro-fibromatosis type 1	Cafe au lait spots, neurofibro-mas, axillary/ inquinal frecklings, Lisch nodules	Optic glioma, malignant peripheral nerve sheat tumour (MNPST)	1:3,500	*NF1*	For opticus glioma other therapy than RT	MPNST observed after RT for optic gliomas but gene-radiation interaction not found
Nijmegen breakage syndrome	Growth deficiency, intellectual deficiency, immuno-deficiency	Lympho-reticular malignancy	Rare	*NBS1*	Reduced dosage/duration of RT if not avoidable	Yes
Retinoblastoma		Retino-blastoma, bone and soft tissue sarcoma	1:20,000	*RB1*	RT induces second cancer development	Yes

Material and Methods: Pubmed was searched for studies between the years 1990–2011 for analyzing in vitro or in vivo the sensitivity to ionizing