

criteria, erythema rating, TEWL, skin hydration, patient's view of itch, pain, acceptance and view of each preparation and adverse events, were monitored; at the final visit patients and investigators expressed their preference for one of the preparations.

Results: MAS065D showed statistically significant superiority in the outcomes of NCI grading for radiation dermatitis at 4 weeks ($p=0.031$; see * on inset figure) and erythema at 4, 5 and 6 weeks ($p=0.01$, 0.005 , 0.03 respectively). Both patients' and investigators' preferences for one of the study preparations were statistically in favour of MAS065D ($p=0.007$ and 0.035 respectively). Very few patients recorded non-zero itch and pain scales, so no significant differences emerged between the two groups. Patient numbers in this pilot study were too low for sub-group analysis of those at high risk of radiation dermatitis (smokers and those with high BMI). **Conclusion:** MAS065D (Xclair™) can provide an effective option for managing radiation dermatitis although further studies are needed. Xclair may provide a useful intervention in patients in which skin management is difficult (e.g. following radiotherapy in head and neck or rectal area).

References

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POSTER

A model of experimental kidney irradiation for screening of response modifiers: evaluation of insulin-like growth factor-1 (IGF-1) and a chemical p53 inhibitor

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Background: The kidney is one of the most radiosensitive abdominal organs. Response modifiers might improve the therapeutic ratio in a variety of common malignant tumors treated with radiotherapy. Therefore, we tested whether IGF-1 or the chemical inhibitor of p53 1-(4-Methylphenyl)-2-(4, 5, 6, 7-tetrahydro-2-imino-3(2H)-benzo) ethanone hydrobromide, also known as pifithrin- α , prevents radiation-induced kidney toxicity.

Material and methods: Adult female C3H mice were treated with single-fraction radiotherapy to the right kidney with doses of 6–17 Gy and with or without two different response modifiers. The kidney function was assessed prior to radiotherapy, 19 weeks thereafter and then every 6 weeks by means of 99mTc-dimercaptosuccinate scans, i.e. static scintigraphy. Maximum follow-up was 12 months. IGF-1 was given subcutaneously either concomitant to radiotherapy or after deterioration of the kidney function, i.e. after 5–6 months. Delayed treatment after deterioration of the kidney function was administered over 4 weeks, immediately followed by repeat scans every 6 weeks. Doses of IGF-1 were 0.5–25 μ g per injection. Pifithrin- α was given prior to radiotherapy.

Results: The function of the irradiated kidney continuously declined during follow-up in all control groups in a dose-dependent fashion. Very accurate and reproducible results were obtained when examining the same control animals several times before the development of kidney dysfunction with this method of static scintigraphy. The maximum deviation was 3% (median 1%). Concomitant treatment with 12 or 15 Gy and IGF-1 significantly reduced the number of mice with a severe decline, defined as loss of function of 50% or more. In contrast to controls, no statistically significant decline of the mean kidney function was observed in the best IGF-1 group. The best dose of IGF-1 was 5 μ g per injection, administered over 2 weeks. Delayed treatment after deterioration of the kidney function was unable to restore the function regardless of the IGF-1 dose. Very few animals in the groups with delayed IGF-1 showed at least stabilisation of the compromised kidney function. Pifithrin- α did not influence the degree of kidney dysfunction.

Conclusions: We have developed a relatively simple, accurate method for screening of response modifiers in the context of mouse kidney irradiation. Our results demonstrate that administration of IGF-1 concomitant to radiotherapy modifies the development of kidney dysfunction. We have examined the IGF-1 dose-response in order to define the optimum treatment schedule. The dose-modifying factor is estimated to range between 1.1 and 1.2, however, further radiation doses will have to be studied. Established renal insufficiency did not improve after prolonged administration of IGF-1, suggesting that early intervention might be the preferable approach.

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POSTER

The influence of TGFB1 polymorphisms on risk of subcutaneous fibrosis after radiotherapy; a study based on DNA from formalin fixed paraffin embedded (FFPE) tissue samples

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Background: In a previously published study based on 41 breast cancer patients, we demonstrated that the TGFB1 position – 509 T/T and codon 10 Pro/Pro genotypes were associated with increased risk of radiation induced fibrosis (R&O 69; 127–135). This investigation was based on DNA from cultured fibroblasts. Similar results have been obtained in two independent studies (R&O 75;18–21 and IJRB 79; 137–43). In order to seek a confirmation of these findings, we validated a method to assess single nucleotide polymorphisms based on FFPE samples, with the intention to extend the study of the TGFB1 SNPs to a larger patient cohort from which only archival histological material was available.

Materials and methods: A validation study was carried out in which three TGFB1 SNPs (position – 509, codon 10 and codon 25) were assessed in 137 patients (R&O 72; 351–356). This demonstrated that a highly reliable genotyping in FFPE could be achieved when the methods for sample selection, DNA extraction and PCR were carefully optimised. Subsequently, the validated genotyping assays were applied to 160 breast cancer patients given post mastectomy radiotherapy in 1978–1982 using two different fractionation protocols. 119 patients did not receive any systemic treatment whereas 41 patients were given CMF chemotherapy. Based on corresponding recordings of absorbed 2 Gy equivalent radiation dose and fibrosis score in three treatment fields per patient, dose response curves for grade 2–3 subcutaneous fibrosis were constructed. Differences in radiosensitivity were quantified in terms of ED50 values and enhancement ratios.

Results: The ED50 for patients given no systemic treatment and CMF were 49.7 and 45.6 Gy respectively and differed significantly from each other (enhancement ratio 1.09, 95% CI 1.04–1.14). Therefore, the influence of the assessed TGFB1 SNPs were analysed separately in these two groups. No significant associations were found between the assessed SNPs and fibrosis risk. Only for the codon 25 SNP, a borderline significant association with fibrosis risk was found in the patients not given systemic treatment. ED50 for the codon 25 Arg/Arg and Arg/Pro genotypes were 50.1 and 45.6 Gy respectively, (enhancement ratio 1.10, 95% CI 0.99–1.22).

Conclusion: The previously observed associations for the TGFB1 position –509 and codon 10 SNPs with risk of radiation induced fibrosis could not be confirmed in this study. Further studies are needed to clarify these conflicting findings.

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POSTER

Improved temporal resolution by a respiratory gated segment reconstruction: towards four-dimensional (4D) radiation therapy for heavy ion beams using the 256-detector-row ct-scanner

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Purpose: To perform more precise treatment planning for respiratory-moving tumors, we developed a respiratory gated segment reconstruction method (RS) based on the Feldkamp-Davis-Kress algorithm (FDK) which can achieve high temporal resolution and high signal-to-noise ratio. We compared full scan (FS-FDK) and RS-FDK with regard to the image quality and the obtained dose distributions for heavy ion treatment planning.

Methods and Materials: Data acquisition for RS-FDK relies on the assistance of the respiratory sensing system in a cine scan mode with a 256-detector row CT. We compared the image quality for RS-FDK to that for FS-FDK in phantom and animal studies. To evaluate the accuracy of the actual irradiation for the moving tumors, we compared the dose distributions of both algorithms in heavy ion treatment planning with the beam parameters of FS-FDK.

Results: RS-FDK provided images without motion artifacts and visualized the edges of the liver and pulmonary vessels more clearly than FS-FDK. With regard to the iso-dose distributions, FS-FDK covered the target volume. RS-FDK, however, had an insufficient dose to the target and a considerable dose was deposited to the normal tissue around the target. Respiratory gated irradiation has already been carried out at HIMAC. The present results pose a problem about the CT images used in treatment planning of the respiratory gated irradiation, though there seems to have been no evidence of increasing local failure so far because of the wide margins applied at HIMAC. The conventional respiratory gated CT

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.

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POSTER

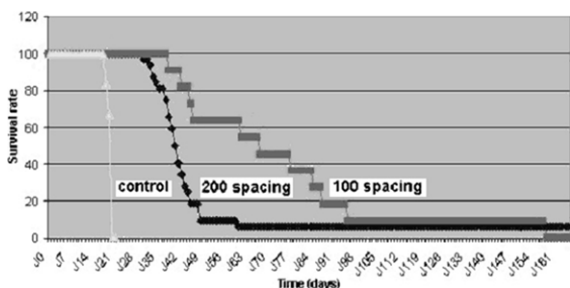
Microbeam Radiation Therapy (MRT) applied to rats' brain tumor: finding the best compromise between normal tissue sparing and tumor curing

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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.

10⁴ 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 × 12 mm² 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.

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POSTER

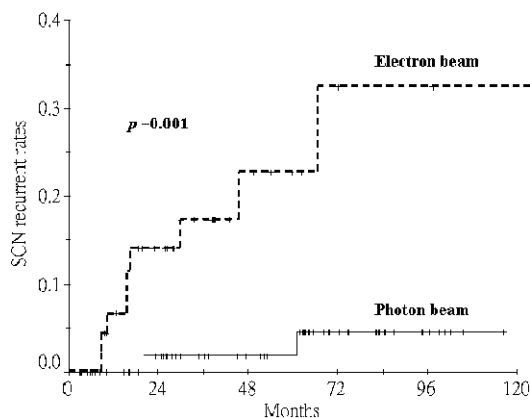
Comparison of locoregional recurrences following postmastectomy radiotherapy using electrons or photons: poor supraclavicular node control of electron beam irradiation in patients with four or more positive axillary nodes

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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 ≥ 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.

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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