Table 1: Measurements in mm

	Bodyfix			Vaclok		
	Median	Min	Max	Median	Min	Max
COM AP	8.2	4.1	10.8	7.9	5.1	16.1
COM SI	4.5	2.1	9.1	4.4	2.1	9.9
Base AP	8.9	4.8	13.8	9.0	6.0	18.1
Base SI	3.8	2.6	7.8	4.9	2.9	8.8
Post AP	7.9	3.0	11.1	8.1	4.8	19.7
Post SI	4.9	2.1	11.7	5.8	2.7	11.1
Apex AP	9.4	1.8	13.5	8.2	6.3	13.5
Apex SI	3.6	2.0	10.8	4.5	1.8	9.6

1364 ORAL

Predicting the radiotherapy service requirements in Scotland in 2015

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Background: Provision of adequate radiotherapy machine capacity is crucial to ensuring optimal cancer care. Therefore, as part of a National Planning process the Scottish Executive commissioned this work to establish the potential requirements over the next decade.
Methods: Firstly, using age-period-cohort regression models the predicted number of cases for the different cancer types that will be diagnosed in 2011–2015 was calculated. Then, using adaptations of models developed by the Australian National Cancer Control Initiative [1], data from a variety of Scottish audits were used to calculate the optimal Scottish radiotherapy utililisation. Finally, all site-specialist Radiation Oncologists in Scotland were surveyed as to their current standard fractionation for each radiotherapy indication and predicted changes in fractionation by 2011–2015.
Results: There is a predicted 18.9% increase in the number of cancer cases (specifically breast +23.4%, lung −9.6%, prostate+35.0%, colorectal+29.0%, head & neck+24.9%). The optimal radiotherapy utilisation for all cancer sites during the initial management phase was 44.2–47.9% but varied from 4% to 78.6% (head & neck 78.6%, breast 70.0%, lung 62.8%, prostate 61.4%) and 5.0 to 5.3% should receive radiotherapy at relapse. Based on current patient numbers and recommended fractionation between 198,000–243,000 fractions are required currently to deliver optimal treatment. With the increase in cancer incidence and predicted changes in fractionation between 242,452–318,422 fractions will be required by 2011–2015. However, to prevent waiting lists demand should represent 90% of capacity, therefore the capacity to deliver between 270,000 and 354,000 fractions per annum will be required.
Conclusions: By 2006 in Scotland, if current machine working practices continue there will be capacity to deliver 234,000 fractions per annum. Therefore over the next decade there needs to be a further significant increase in the numbers of fractions of radiotherapy available, for optimal cancer treatment. Further work is ongoing on how best to meet this demand.

References

[1] http://www.ncci.org.au/pdf/radiotherapyreport.pdf

Poster presentations (Mon, 31 Oct)
Radiotherapy and radiobiology

1365 POSTER

Modulation of tumor cell radiosensitivity by native immune cells: the role of interferon-ã in iNOS mediated radiosensitization

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Background: Hypoxia and the pro-inflammatory tumor infiltrate are two factors of the tumor microenvironment, which underlie tumorigenesis and generally correlate with poor prognosis. It is well known that hypoxia directly impairs the radiosensitivity of tumor cells, while the impact of immune cells remains unclear. In this study, we examined the radiomodulatory effects of native immune cells on hypoxic tumor cells. We hypothesized that activated immune cells may secrete interferon-γ (IFN-γ), which may induce the production of the radiosensitizer NO inside tumor cells through the iNOS pathway. To activate immune cells, clinically relevant concentrations of lipid A and IL-12+IL-18 were used.
Material and methods: Native immune cells were isolated from the spleen of Balb-c mice and were activated for 24h with lipid A (3 μg/ml) or with IL-12 (3 ng/ml) + IL-18 (30 ng/ml) to produce conditioned medium (CM). The CM was analyzed for IFN-γ production by ELISA and diluted 10 times with fresh medium to apply on EMT-6 mammary carcinoma cells. All treatments were performed in 1% oxygen, modeling the hypoxic tumor microenvironment. The induction of nitric oxide synthase (iNOS) in the tumor cells was analysed by RT-PCR, Western blotting and nitrite accumulation. The tumor cells were irradiated in a model of metabolic hypoxia and cell survival was measured by a colony formation assay.
Results: Activated spleen cells secreted a high level of IFN-ã, up to 1750 pg/ml/24h. The induction of IFN-ã was confirmed at the transcriptional level by RT-PCR, using an ABI PRISM 7000 sequence detection system and predeveloped assays on demand. The CM from activated spleen cells induced iNOS in EMT-6 tumor cells, resulting in the accumulation of the oxidative NO metabolite nitrite, up to 36 μM/24h. The induction and resulting enzymatic activity of iNOS were abrogated by more than 50% by a neutralizing IFN-γ antibody. The induction of iNOS resulted in a significant hypoxic tumor cell radiosensitization, with an enhancement ratio of 2.2. This radiosensitization was abrogated by the metabolic iNOS inhibitor aminoguanidine and inhibited by more than 50% by a neutralizing IFN-γ antibody.
Conclusions: Activated spleen cells radiosensitize hypoxic tumor cells through the production of IFN-γ, which induces the production of the radiosensitizer NO inside tumor cells. Therefore, the pro-inflammatory tumor infiltrate represents a novel target for radiosensitizing strategies.

1366 POSTER

A double-blind, randomised, placebo-controlled clinical study to evaluate a topical hyaluronic acid-based, hydrolipidic treatment for radiation dermatitis

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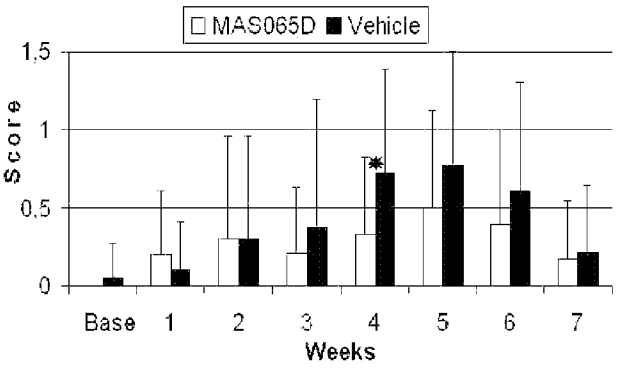
Background: Radiation damage associated with radiotherapy reduces quality of life for patients, particularly where there is moist desquamation (up to 10% of patients [1]. There are no widely available commercial preparations with clinically proven benefit in the management of radiation dermatitis. This study was designed to assess the efficacy and tolerability of a new preparation, MAS065D, in the management of radiation dermatitis in patients receiving radiotherapy for breast cancer.
Methods and materials: MAS065D (Xclair™, Sinclair Pharmaceuticals Ltd) is a hydrolipidic topical preparation designed to reduce the skin reactions that follow radiotherapy by increasing hydration and dampening down the cascade of damage arising from free radicals and enzymes released within irradiated skin, thereby helping to preserve skin integrity. The vehicle control had only emollient properties, and did not contain hyaluronic acid or other key ingredients.



NCI Grading

Twenty patients were randomised blindly to use the two study preparations, three times daily, on separate sections of the irradiated skin, throughout the duration of radiotherapy and for two weeks afterwards. Patients were monitored before therapy, weekly during therapy, and for two weeks after radiotherapy was completed. Skin appearance according to NCI toxicity

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

[1] Porock D, Kristjanson L. *Eur J Cancer Care* 1999;8(3):143–53.

1367 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 pififthrin-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-dimercaptosuccinat 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 μg per injection. Pififthrin-alpha 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 μg 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-alpha 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.

1368 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.

1369 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