collections/questionnaires per patient varied from 1 to 11 (median: 6). In both the pre-RT and post-RT settings, there was strong correlation between saliva flow rates, RTOG toxicity scores, and most questionnaire responses. There was no measured correlation between flow rates (stimulated or unstimulated) and pilocarpine use. The relationship between speech toxicity and saliva flow rates was variable: In the pre-RT time period, there was strong correlation between toxicity and both stimulated ($p = 0.04$) and unstimulated ($p<0.01$) saliva flow rates. In the post-RT follow-up period, there was weak correlation between stimulated saliva flow rates and toxicity ($p = 0.06$), and no correlation between unstimulated flow and toxicity ($p = 0.3$).
Conclusion: There is strong correlation between most quality of life endpoints, RTOG toxicity, and stimulated and unstimulated saliva flow rates, which makes the sparing of salivary tissue a worthwhile planning goal in head and neck IMRT treatments. We did not observe a statistically significant relationship between post-RT saliva flow rates and speech toxicity.

1361 ORAL

Dose reduction to the heart with respiratory gated radiotherapy

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Purpose/Objective: Because there are hints for an increased risk of cardiovascular diseases after radiotherapy of the left chest wall the dose to the heart should be reduced as far as possible. With respiratory gating technique irradiation can be restricted only in the inspiratory plateau phase and so the distance between heart and chest wall will be increased. As a result the dose to the heart, in particular to the anterior wall, can be reduced. We investigated in all patients with left sided breast cancer dose reduction to the heart when treated only in the inspiration phase compared with not gated treatments.
Materials and methods: Between Sep. and March 2005 32 patients with left sided breast cancer were treated with respiratory gating technique based on a retrospective 4D CT scan. With this technique we irradiate only in maximum inspiration with a range between 10%-20%. For the investigation of real dose reduction to the heart we performed for all of these patients a normal and a respiratory gated planning CT. Planning was done with the same treatment parameters in both CT. DVH for the entire heart and the anterior left ventricle wall were calculated. All of these patients were treated with 2 Gy single dose to a total dose of 50 Gy to the entire left breast/chest wall. 18 patients had an additional boost of 10 Gy. The PTV was in 36 patients after breast conserving surgery the left breast, in 6 patients after mastectomy the left chest wall.
Results: The mean dose to the entire heart was 1.7 Gy (0.5 Gy-3.2 Gy) without and 0.8 Gy (0.5 Gy-2.0 Gy) with respiratory gating ($p = 0.03$). To mean dose to the anterior ventricle wall was 7.1 Gy (0.9 Gy-15.3 Gy) without and 2.4 Gy (0.7 Gy-6.0 Gy) with respiratory gating ($p = 0.003$). The mean maximal dose to the anterior wall was 40.6 Gy (27.3 Gy-53.6 Gy) without and 24.9 Gy (1.9 Gy-42.3 Gy) with respiratory gating ($p = 0.001$). For the 26 pat after breast conserving surgery the mean doses to the anterior wall was 7.5 Gy in the non gated compared to 2.4 Gy in the gated group. After mastectomy the doses were 6.5 Gy (non-gated) and 3.1 Gy (gated).
Conclusions: Respiratory gating and irradiation only in the inspiratory phase reduce radiation dose to the heart and especially to the anterior wall of the heart significantly.

1362 ORAL

To pee or not to pee? A randomized study of Full vs. Empty Bladder instructions during prostate radiotherapy and its impact on organ motion and targeting accuracy

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Objective: To determine whether bladder filling (full vs. empty) instructions during radiotherapy (RT) affects inter-fractional prostate motion and targeting precision during a 7-week course of radical conformal RT.
Method: 34 patients with T1-T2 prostate cancer undergoing routine 3D RT (4-field, 70 Gy/35#/7 weeks) were randomized to either full bladder (500 mL water 1 hr before treatment) or empty bladder instruction for the entire treatment course. TRUS-guided insertion of three gold markers into the prostate was done prior to treatment planning. Routine patient set-up by bone-anatomy verification and correction was performed during first week of treatment. Thereafter, twice-weekly orthogonal aSi-EPI images were taken to measure set-up error (image mismatch on bone) and targeting error (mismatch by gold markers). Prostate motion was determined as the arithmetic difference between set-up error and targeting error. All images were analyzed by one expert user of Varian Vision software.
Results: Eighteen and 16 patients were randomized to full and empty bladder set-up respectively. No significant difference in inter-fractional prostate motion and targeting error was observed (Table 1). However, absolute prostate motion >5 mm in the sup-inf direction was seen in 13% of 422 images analyzed for all patients. Targeting error >5 mm was observed in 19% of 424 images. Prostate motion and set-up error both contributed to targeting variability, which remained constant during the 7-week course treatment. No difference in treatment-related bladder or rectal morbidity has been observed (median F/U 12 months).

Table 1: Measurements of prostate motion and targeting accuracy on patients treated with either full or empty bladder instructions

Measurement	Bladder Instruction	Median Standard Deviation		
		Right-Left	Ant-Post	Sup-Inf
Prostate motion	Full (n = 18)	0.7 mm	1.9 mm	1.9 mm
	Empty (n = 16)	0.5 mm	1.7 mm	1.7 mm
Targeting variability	Full (n = 18)	2.0 mm	2.6 mm	2.3 mm
	Empty (n = 16)	1.9 mm	2.6 mm	2.2 mm

Conclusions: Inter-fractional prostate motion and targeting accuracy were not influenced by bladder filling instructions given to patients. Improvement of treatment precision to within 5 mm will likely require daily pre-treatment target-imaging with table adjustments.

1363 ORAL

A randomised study to investigate the role of abdominal compression in prostate intrafraction motion

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Background: Intrafraction prostate motion may contribute to target volume underdosage when using small PTV margins. Abdominal compression may decrease intrafraction motion by reducing respiratory effect. Therefore, to evaluate the role of abdominal compression in prostate intrafraction motion we performed a randomized study using 2 different immobilization devices, one of which incorporated a component to reduce abdominal movement (Bodyfix).
Methods: 32 patients receiving conformal radiotherapy (RT) for localized prostate cancer (PTV = 7 mm post and 10 mm elsewhere) provided informed consent and were assigned to Vac Lok (n = 16) or Body Fix (n = 16). All patients had daily on-line correction of interfraction errors of $\geqslant$3 mm using electronic portal imaging (EPI) of implanted fiducial markers (at the apex, posterior and base) as a surrogate for prostate position. During every 4th fraction of RT, EPI's were also taken at the start and end of the first and last lateral beams. Absolute maximum displacements from the planned position for each EPI were measured for centre of mass (COM) and individual markers.
Results: A total of 1242 images were reviewed, taken an average of 10 fractions per patient, distributed over their course of treatment. The mean time between the first and last EPI was 6.5 min (range 3.5 to 14.5). The displacements measured from the EPI's are shown in table 1. There were no statistical differences in displacements of the COM or markers with or without abdominal compression at the 5% confidence level (Mann Whitney U-test).
With current PTV margins, absolute maximum displacements from the planned position would have resulted in target underdosage in $\leqslant$1.6% of fractions analysed. Absolute maximum displacements from the planned position incorporate both intrafraction prostate motion and the residual displacements after the application of online correction strategies. When these residual errors were mathematically eliminated from the measured displacements, intrafraction prostate motion would have resulted in target underdosage in $\leqslant$1.4% of treatment fractions.
Conclusions: When using the Bodyfix system, abdominal compression produced no statistically significant effect on intrafraction motion of the prostate. Our current PTV margins appear to adequately encompass both inter and intrafraction prostate displacements in more than 98% of patients. With daily online image guidance and correction protocols, intrafraction prostate motion appears to be the major contributor to residual errors and possible target underdosage.

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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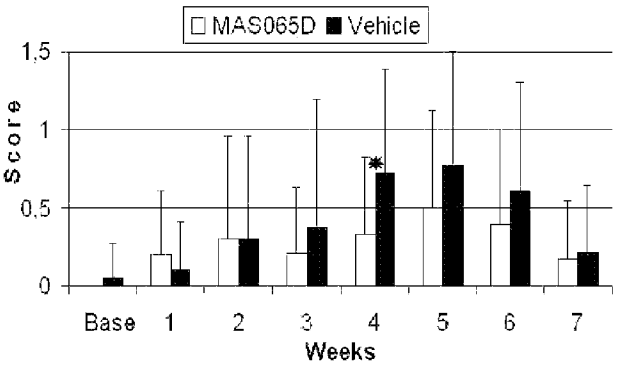
Background: Radiation damage associated with radiotherapy reduces quality of life for patients, particularly where there is moist desquamation (up to 10% of patients [1]. There are no widely available commercial preparations with clinically proven benefit in the management of radiation dermatitis. This 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