to assess any differences in these anatomical sub-regions. The spatial relationship was analyzed with respect to points of interest placed at the extreme margins boundaries of the two GTVs i.e. superior, inferior, anterior and posterior. The difference in cm between the CT-GTV and M-GTV points of interest co-ordinates was calculated to quantify the spatial differences.
Results: The mean overall CT-GTV/M-GTV volume ratio for the entire tumor was 1.2 (range 0.5 to 2.9). For the portion of GTV in the true rectum the mean ratio was 1.3 (0.8–2.9) and recto-sigmoid was 1.6 (0.4–4.6). Only one patient had a portion of GTV present in the anus and this was only visible on MRI. With respect to the spatial comparison, the CT-GTV minus M-GTV values showed a mean difference for the superior margin of 0.19 cm (range −2.0 to 4.0 cm), for the inferior margin 0.49 cm (range −3.0 to 4.0 cm), for the anterior margin −0.35 cm (−5.7 to 1.95 cm) and for the posterior margin −0.15 cm (−0.93 to 0.77 cm). Underestimation of the GTV by CT compared to the M-GTV occurred in two patients and was highlighted by volume differences in the sigmoid and with the spatial differences in the anterior and superior boundaries. Overestimation of the GTV by CT could occur in the true rectum or sigmoid and is usually due to faeces in close proximity to the tumor.
Conclusions: CT defined target volumes can provide a reasonable estimate of the GTV compared to MRI but in some cases there is substantial over- and under-estimation of the GTV. Overestimation by CT results primarily from faeces in close proximity to the tumor. Underestimation and potential geographic miss using CT results from difficulty in visualizing the extent of tumor invasion within the sigmoid colon and anus. The use of MRI may avoid these potential problems.

1412 POSTER

Interfractional lung tumour and oesophageal movement using Active Breathing Control (ABC) during fractionated radical radiotherapy (RT)

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Introduction: Concomitant chemo-radiation appears to result in a survival advantage in patients with Non-Small Cell Lung Cancer (NSCLC) compared to sequential therapy, at the expense of increased radiation-induced pulmonary and oesophageal toxicity. RT planning takes into account tumour movement by adding a margin to the Gross Tumour Volume (GTV) called the Planning Target Volume (PTV). We aimed to immobilise the tumour with ABC to consider PTV margin reduction and assess the extent of oesophageal movement on radiation dose delivered to the oesophagus before introducing techniques to avoid it.
Method: 16 NSCLC patients had CT scans using an ABC device (William Beaumont Hospital, USA) in the first, middle and final week of RT. CT images were registered using bony anatomy. Change in the GTV with treatment was recorded. The GTV centre of mass was defined by the planning system using a spherical method. In 7 patients, the oesophagus was contoured and the position of the oesophageal borders relative to fixed bony anatomy was measured at 4 cm intervals. Displacement of the GTV centre of mass and oesophageal borders relative to the first scan provides a measure of movement.
Results: 12/16 (75%) of patients tolerated ABC for 3 scans. 4 were excluded from the analysis (2 progressed, 2 did not tolerate ABC). Mean reduction in the GTV was 34% by the 3rd CT. Mean displacement and standard deviation (SD) of the GTV and oesophagus is shown in the table. Results quoted are in relation to the first scan.

Direction of displacement	Mean displacement and Standard Deviation (SD) in mm		
	Right–left	Anterior–posterior	Superior–inferior
GTV scan 2	1.4 (1.7)	1.6 (1.8)	1.7 (1.6)
GTV scan 3	1.2 (0.6)	1.7 (1.4)	2.9 (2.4)
Oesophagus scan 2	Right 2.4 (3.2)	Anterior 2.1 (2.7)	–
	Left 2.1 (2.7)	Posterior 2.1 (2.7)	–
Oesophagus scan 3	Right 1.8 (2.8)	Anterior 1.9 (2.6)	–
	Left 2.1 (2.8)	Posterior 1.7 (2.1)	–

GTV displacement was greatest in the superior-inferior direction for the 3rd scan as 2 patients had resolution of collapse distal to the GTV causing a shift in position up to 7.7 mm in this direction. Oesophageal movement varied along its length, more marked at the level of the carina and gastro-oesophageal junction and less marked at the thoracic inlet. The mean SD of oesophageal displacement over all levels was 1.6 mm.
Conclusion: ABC was well tolerated at 3 time points during RT. Incorporation of movement of the GTV and oesophagus with ABC into standard margin calculations may allow reduction of dose to the lung and oesophagus reducing the risk of radiation-induced toxicity.

1413 POSTER

Normal tissue radiation sensitivity in cancer patients undergoing radiotherapy

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Background: Very serious radiation-induced side effects will develop in about 5–10% of cancer patients undergoing radiation therapy. The aim of our experiments is to establish screening methods to identify radiation sensitive patients before the onset of radiation therapy.
Material and methods: Blood samples and skin biopsies were taken from cancer patients undergoing radiation therapy. The in vitro radiation sensitivity of peripheral blood lymphocytes was studied by single-cell electrophoresis (comet) and micronucleus assays. Primary fibroblast cultures were established from skin biopsies and the radiation sensitivity of fibroblasts was investigated by comet assay and by determining the survival fraction after 2 Gy irradiation (SF2 value). The in vitro data were correlated to the clinical symptoms of the patients. The gene expression patterns of radiation sensitive and resistant patients were studied by Agilent's whole human genome micro array system containing 44000 human genes.
Results: The comet and micronucleus assays were not informative. The SF2 values of control patients ranged between 26–40%. The SF2 values of patients with radiation-induced late toxic reactions in the central nervous system moved toward lower ranges and peaked between 8–15%. Similar alterations have been observed in patients with early and late radiation-induced toxic reactions in the skin and mucosa. There the SF2 values peaked between 15–20%. The gene expression analysis revealed genes responsible for radiation response in human fibroblasts and different expression patterns were detected in radiation sensitive and resistant patients.
Conclusions: In vitro assay might be applied to estimate the radiation sensitivity of cancer patients before the start of radiation therapy. This might be used for the individualization of radiotherapy protocols.

1414 POSTER

Induction of fluoropyrimidine metabolizing enzymes after an exposure of a cancer cell to an ionizing radiation – a concept supporting continuous schedules of chemoradiotherapy

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Background: Chemoradiotherapy employing fluorinated pyrimidines is a standard treatment approach although the exact mechanism of mutual potentiation has not been fully clarified. The original concept of an induction of fluoropyrimidine anabolizing enzymes within a post-radiation reaction was introduced in early 90th years. With the aim to establish a time dependence between a radiation dose (fraction) and maximal fluoropyrimidine efficacy a series of experiments was performed assessing the development of both the transcripts and proteins of fluoropyrimidine metabolizing enzymes after a single dose of radiation.
Material and methods: HeLa cells were irradiated by a dose of 200 cGy followed by an array of assessments mRNA encoding thymidine phosphorylase (TP), thymidine kinase (TK), thymidine synthetase (TS) and dihydropyrimidine dehydrogenase (DPD). A real time PCR method was employed using beta-actin (BA) as a reference gene. When mRNA induction was proved, an array of TP, TK, TS and DPD assessments was planned accordingly. A Western blot analysis was performed using specific commercially available antibodies. The time intervals between radiation and onset of increased enzyme concentration were established.
Results: The TP, TS and DPD mRNA levels decrease early after the radiation. A strong increase follows from the 5th hour after the radiation. There is a short early increase of TK mRNA 10 minutes after the radiation, however 5 hrs. later the development is similar to other enzymes. The mRNA levels increase 2–6 fold. The protein levels of TP, TS and DPD

increase from 24 hrs. after the radiation. The increase is up to 5–6 fold and lasts for more than 96 hrs. after the radiation. TK increase is less apparent, up to 2-fold, with a similar time to onset 24 hrs. and also long lasting, more than 96 hrs. A TP/DPD ratio may be roughly established, in a range of relative values 2–3 indicating that anabolism of fluorinated pyrimidines to active forms exceeds catabolic inactivation.
Conclusion: Both mRNA and protein assessments confirm the concept of an enhanced anabolic activation of fluorinated pyrimidines after an ionizing radiation. The catabolic inactivation is less strongly activated than anabolism. The enhancement is long lasting, more than 96 hrs. Therefore any timing of either daily radiation fractions or pyrimidines administrations does not seem rational. The long lasting predominanat enhancement of pyrimidines anabolism supports the currently used continuous infusion for the entire radiation period.

1415 POSTER

Distortion corrected T2 weighted MRI: implications for rectal and bladder dose sparing in prostate radiotherapy planning

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Purpose: To evaluate distortion corrected MRI as a radiotherapy planning tool for prostate cancer and assess possible rectal and bladder dose sparing as compared to CT.
Methods: Eleven men who were to be treated with radical conformal radiotherapy for localised prostate cancer had, in addition to their planning CT scan, an MRI scan under radiotherapy planning conditions, which was then corrected for geometric distortion. Radiotherapy plans were created for planning target volumes (PTV) derived from both the MRI and CT defined prostate. The bladder and rectum were defined as solid organs. The PTV consisted of the prostate and a symmetrical 5 mm margin. To treat the PTV, a plan comprising an anterior and two wedged lateral fields was used with blocks for beam shaping. The same wedge angles and beam weightings were used for MRI and CT derived plans for each patient. The PTV was treated to a notional 70 Gy in 35 fractions for each plan. Dose volume histograms were produced for the rectum and bladder.
Results: The mean volume of the prostate as defined on CT and MR was 41cc and 36cc respectively ($p = 0.009$). The mean rectal volume as defined on CT and MRI was 87 cc and 94 cc respectively ($p = 0.56$). The mean volume of the bladder as defined using CT and MRI was 284 cc and 261 cc respectively ($p = 0.5$). The predicted dose to the rectum (as defined using MRI) from plans treating each PTV is shown below. For the same dose levels, there was no difference in the proportion of bladder (as defined using MRI) receiving a given dose between plans.

Mean percentage of rectum treated to given dose.

dose	PTV CT prostate	PTV MR prostate	p value
45 Gy	23	18	0.05
50 Gy	21	16	0.05
55 Gy	19	15	0.04
60 Gy	17	12	0.03
65 Gy	14	8	0.04
70 Gy	2	1	0.08

Conclusion: Distortion corrected MRI is feasible and for the prostate, results in a smaller target volume than CT. This leads to a lower predicted proportion of the rectum treated to a given dose than with CT.

1416 POSTER

Possibility of laser-accelerated proton beams in radiotherapy

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Background: The purposes of this study are (i) to investigate distinctive features of laser ion accelerators from a clinical standpoint; (ii) to list the problems to solve when applying the accelerator to clinical setting; (iii) to simulate radiation treatment with a laser-accelerator under the condition of the currently available energy regime for eye diseases; (iv) to show future possibilities for radiotherapy with laser-accelerated proton beams.
Material and Methods: We participated in several meetings involving radiation oncologists, physicists, radiotherapy technologists under the auspices of JST and JAERI since 2003. We discussed and reviewed the related literature with the aim of developing laser-accelerated proton therapy. This is an interim report. We also developed simulation tools for laser-accelerated proton therapy: they include (1) particle-in-cell simulation (PIC) software which calculates the properties of laser-accelerated protons, (2) Monte-Carlo simulation software for dose calculations in a human body, and (3) visualization tools for the dose evaluation. We attempted to simulate laser-accelerated proton therapy for the eye diseases (uveal melanoma and age-related macular degeneration).
Results: A laser ion accelerator is expected to be compact, simple, and low cost. These features are remarkable in comparison with synchrotron or cyclotron accelerators. A laser ion accelerator has another obvious advantage of generating narrow proton beams. This feature makes it possible to treat minute targets precisely. The maximum energy of laser-accelerated protons is correlated to the laser intensity. In addition, laser-accelerated proton beams are not parallel, but diverging. In experiments, the maximum proton energy is up to several tens of MeV, and the energy spectra with a single-layer metal target are broad. It is also necessary to develop techniques to remove particles other than protons (heavy ions, electrons, gamma-rays, neutrons, etc), which are also emitted from the target. With our computer simulation, we demonstrate that eye-ball disease may be treated by the laser ion accelerated proton beams. In future, we will seek optimal parameters of laser accelerated protons.
Conclusions: There lie several problems for clinical usage with the currently available parameters; however, we can recommend that laser ion accelerator with these parameters is suitable for a minute target such as diseases within eyeball.

1417 POSTER

Re-irradiation: analysis of consecutive patients

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Background: Our aim was to analyze the results and evaluate the prognostic factors in the re-irradiation of recurrent/second primary tumors. Patients and Methods: One hundred and six patients (119 lesions) who underwent re-irradiation between June 1997 and February 2005 at the European Institute of Oncology, Milan, Italy, were retrospectively analyzed. There were 62 females and 44 males with median age of 60 years (range 22–91). Primary diagnosis included breast in 27% of patients, followed by lung cancer (20%), head and neck cancer (17%) and other primaries (36%). Re-irradiation was performed for nodal/metastatic lesions, recurrent tumor and for new primary in 84 (70%), 33 (28%) and in 2 lesions (2%), respectively. Twenty eight lesions (24%) were re-irradiated with curative intent, whereas 91 lesions (76%) re-irradiation had palliative intent. The re-irradiation dose varied from 4 to 60 Gy. Three-dimesional conformal radiotherapy (3D-CRT) was used to treat 62 lesions (52%), stereotactic radiotherapy (SRT) was used in 40 lesions (48%) and in 3 cases brachytherapy was added to 3D-CRT or SRT.
Results: Median follow-up was 10 months (range, 1–59 months). Response to treatment was observed in 71% and 63% of patients treated with curative and palliative intent, respectively. Progression was seen in 18% and 19% of patients treated with curative and palliative intent, respectively. Eleven per cent and 18% of patients among two groups were