Results: After a mean f/u of 105 months the rate of LR at 10 years was 12.0%, and the DFR was 70.8% in this young patient set. Age was not a significant cut point for either endpoint. For LR the n-ratio was the first cut point (table A) at 16%, followed by PR status. For DFR there was a dramatically low cut point in n-ratio of 9%, followed by tumor location and T-stage (table B).
Conclusion: We hypothesize that after BCS, ST and RT, subgroups of young patients are at higher risk, determined mostly by the n-ratio, not number of positive nodes. Higher risk is also indicated for medially and centrally located tumors, in PR negative patients and in women presenting with T2 N pos tumors. These subgroups may need a more aggressive therapy. The present results differ from most published reports, where lymph node status is not found critical to the likelihood of local recurrence.

906 ORAL

An interobserver study comparing CT and MRI for GTV delineation in radiotherapy for cervical cancer

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Background: This study evaluated the interobserver and intermodality variation using CT and MR imaging for delineation of gross tumour volume (GTV) in cervical tumours.
Methods: 4 observers (2 radiation oncologists and 2 radiologists) with specialisation in gynaecological oncology outlined the GTV independently on contrast-enhanced CT and MRI scans of 18 patients with cervical cancer. The scans were co-registered and areas of spatial difference between observers and modalities were determined. The volume common to all observers on each scan (V_{com}) and the total encompassed volume (V_{tot}) were measured to assess interobserver variation.
Results: *Intermodality comparison*: The mean tumour volume with CT was 133.9 cm^3 (range 28.2–422.5, SD 119.4) and 73 cm^3 (range 9.4–236 cm^3, SD 74.7) using MRI. The average CT/MRI ratio was 2.5 (SD 1.4), and in all cases the CT volume was larger than with MRI. There was greater interscan variation with smaller tumours, with CT/MRI ratio 3.1 for tumours <50 cm^3 on MRI compared to a ratio of 1.6 for volumes >50 cm^3. The largest discrepancy between modalities was in the superior-inferior directions, with large variation in contours involving the uterine body and vagina. For smaller tumours the entire cervix was often outlined on the CT images due to observer uncertainty.
Interobserver variation: The V_{tot}/V_{com} ratio was 3.3 (SD 1.6) for CT and 3.7 (SD 2.4) for MRI. For all 36 scans, the V_{com} was always smaller than smallest individual observer volume. The interobserver variation was greatest for smaller tumours, with ratio 4.8 for tumours <50 cm^3, and 1.9 for volume >50 cm^3 on MRI, and 4.1 for tumours <100 cm^3 and 2.5 tumours >100 cm^3 on CT. The average ratio between the individual volume and mean tumour volume (and SD), was 0.9 (0.3), 1.0 (0.3), 1.1 (0.2), 1.0 (0.2) for CT, and 0.7 (0.2), 1.2 (0.3), 1.2 (0.3), 0.9 (0.1) for MRI for observers 1, 2, 3 and 4 respectively.
Conclusion: The GTV was on average 250% larger on CT compared to MRI. The MRI scans were particularly useful for defining uterine and vaginal extent of disease. There is large interobserver variation, which has similar magnitude with both CT and MRI, and is greatest with small tumours. This variation should be taken into account when defining GTV, which is increasingly required for planning an integrated boost with IMRT and for 3D brachytherapy.

907 ORAL

Dose escalation with simultaneous integrated boost intensity-modulated radiotherapy for cervical cancer – impact of interfractional organ motion

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Aims: To assess whether the dosimetric advantage of IMRT compared to conformal radiotherapy (CRT) in reducing normal tissue doses is maintained throughout a course of radiotherapy, and that target volume definition is sufficient to account for interfractional movement. In addition, the feasibility of dose escalation with simultaneous integrated boost (SIB-IMRT) to be used in conjunction with intrauterine brachytherapy was evaluated.
Methods: 10 patients with cervical cancer had an RT planning CT scan, and 2 additional scans in the 2nd and 4th weeks of treatment. GTV, CTV and normal structures were outlined on all 30 scans. SIB-IMRT plans were produced to deliver 54, 58 and 60 Gy to PTV1 (GTV+5 mm) and 50.4$_{eq}$ Gy to PTV2 (CTV+15 mm). These were compared to delivering standard dose 50.4 Gy to PTV2 with CRT and IMRT. Treatment fields were applied to subsequent scans, and the impact of organ motion on dose to GTV, CTV and normal tissues were assessed.
Results: On the initial scans, normal tissue receiving >50.4 Gy with CRT, IMRT and SIB-IMRT (60 Gy) respectively were: bladder: 35%, 21%, 30%; rectum: 29%, 24%, 31%; large bowel: 43 cm^3, 12 cm^3, 14 cm^3; small bowel: 138 cm^3, 27 cm^3, 51 cm^3. The mean GTV volume reduced from 68 cm^3 to 59 cm^3, 53 cm^3, and the CTV from 656 cm^3 to 610 cm^3, 576 cm^3 in weeks 2 and 4 respectively. Coverage by 95% isodose of GTV, CTV was: CRT 100%, 99.6% and IMRT 99.9%, 99.5% in week 2; CRT 100%, 99.4% and IMRT 100%, 99.3% in week 4. SIB-IMRT$_{60}$ mean tumour dose was 59.9 Gy, and 93.9% GTV received >57 Gy. Normal tissue doses on repeat scans with CRT, IMRT and IMRT-SIB were: bladder: 33%, 24%, 31%; rectum: 22%, 18%, 26%; large bowel: 77 cm^3, 30 cm^3, 41 cm^3; small bowel: 144 cm^3, 52 cm^3, 64 cm^3 in week 2, and bladder: 36%, 32%, 36%; rectum: 37%, 28%, 35%; large bowel: 79 cm^3, 42 cm^3, 52 cm^3; small bowel: 189 cm^3, 88 cm^3, 99 cm^3 in week 4.
Conclusions: IMRT reduces dose to normal structures by up to 40% on the initial scan. SIB-IMRT can increase the external beam dose to tumour by 20% whilst maintaining normal tissue doses less than with CRT. With interfractional movement, there is increased normal tissue doses with all techniques, but IMRT and SIB-IMRT still irradiate less normal tissue than CRT. The selected CTV-PTV margin is sufficient to ensure adequate dose to GTV and CTV throughout treatment.

Poster presentations (Wed, 26 Sep, 14:00−17:00)
Radiotherapy/radiobiology

908 POSTER

The up-regulation of Integrin Linked Kinase in oral epithelium (mouse) by fractionated irradiation is accelerated by Keratinocyte Growth Factor (Palifermin)

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Background: Early radiation effects in oral mucosa are a severe and often dose-limiting side effect of radiotherapy for advanced head-and-neck tumours. The regeneration response to daily fractionated irradiation, summarized as "repopulation", occurs with a delay of about 1 week after the first fraction, and subsequently results in an increase in mucosal radiation tolerance with increasing overall treatment time. The present study in mouse tongue mucosa was initiated to determine changes in the expression of Integrin Linked Kinase (ILK) during fractionated irradiation, and their modulation by administration of Keratinocyte Growth Factor. ILK links integrins with growth factor receptors and thus modulates intracellular signal transduction. Variations in ILK expression hence may contribute to the regulation of the repopulation processes.
Materials and Methods: Daily fractionated irradiation with 5 X 3 Gylweek was given to the snouts of mice over a total of 2 weeks. In an additional experimental arm, Keratinocyte Growth Factor (Palifermin) was administered as a single injection of 15 mg/kg at the day before the first fraction. Groups of 3 mice per day were sacrificed from day 0 to 16, and the tongues were processed for immunohistochemistry. ILK expression was analysed semi-quantitatively using an arbitrary score for the staining signal.
Results: Compared to un-irradiated controls, an increase in the expression of ILK was found at the end of the first treatment week, i.e. in coincidence with the onset of repopulation. Administration of Palifermin on day −1 resulted in an almost immediate stimulation of ILK expression already on day 0, which remained elevated during the entire first week of irradiation, before a return to control values was observed at the beginning of week 2.
Conclusions: Fractionated irradiation results in a delayed increase in the expression of ILK in oral epithelium, indicating a regulatory role of this protein in the mucosal regeneration response. The earlier stimulation of ILK expression by KGF suggests that this growth factor modulates the intracellular signal transduction via this pathway, eventually resulting in increased mucosal tolerance to fractionated irradiation.
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909 POSTER

Updated results of high dose proton beam therapy (PBT) for stage I non-small cell lung cancer (NSCLC)

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Background: Proton beam has a distinctive depth-dose curve that enables us to deliver higher doses to the tumor without increasing doses to the

surrounding normal tissues. We retrospectively evaluated the safety and efficacy of high dose proton beam therapy (PBT) in patients with stage I non-small cell lung cancer (NSCLC).
Material and Methods: Between December 1999 and September 2006, 77 patients with stage I NSCLC were treated by PBT in our institution. The indication of PBT were (1) clinical stage I NSCLC, (2) PaO2 > 60 torr, (3) medically inoperable, or refusal of surgery, (4) performance status 0−2, (5) written informed consent. The target volume was defined as the gross tumor volume plus appropriate margins for subclinical tumor extension, set-up error and respiratory motion. Treatment was performed using respiratory gating. A total dose of 70−94 Gy_E was delivered in 20 fractions over 4 to 5 weeks. Kaplan-Meier method and CTC-AE version 3.0 were used to assess survival and toxicity.
Results: Patients characteristics were as follows: median age 75 years (range, 52 to 87); male/female, 54/23; Stage IA/IB, 43/34; squamous/adenocarcinoma/others, 28/23/26; total dose 70/80/88/94 Gy_E, 3/57/16/1. The initial response rate was 74% (95% confidence interval (CI), 63 to 83%). With a median follow-up period of 24 months (range, 3 to 82 months), the 2-year local progression-free and overall survivals were 94% (95%CI, 87 to 99%) and 91% (95% CI, 83 to 99%), respectively. No severe acute toxicity was observed. Late grade 2 and grade 3 pulmonary toxicities were observed in 5 and 3 patients, respectively. Four patients experienced fractures of ribs within irradiated volume. The 2-year loco-regional progression-free survivals in stage IA and IB patients were 95% (95% CI, 88 to 100%) and 67% (95% CI, 50 to 84%), respectively. Six of 8 patients who suffered late grade 2 or greater pulmonary toxicities had stage IB disease.
Conclusions: Updated results shows that PBT is a promising treatment modality for stage I NSCLC, although loco-regional recurrences and late pulmonary toxicities in stage IB patients were substantial. Further investigation of PBT for stage I NSCLC is warranted.

910 POSTER

MVCT image-guidance for abdominal and retroperitoneal IMRT target volumes

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Purpose: Mega-voltage CT (MVCT) image-guidance afforded by the TomoTherapy HiArt helical tomotherapy system provides limited soft-tissue contrast and has not been evaluated with regard to its utility in localizing upper abdominal and retroperitoneal soft-tissue radiation target volumes. We analyzed automated system generated patient translational and rotational corrections to match simulation target setup based on mutual information fusion (MI), and evaluated if the MVCT image quality was sufficient to judge the accuracy of MI image-fusion. We assessed how often subsequent user interaction was needed for optimized target setup and compared MI fusion derived positional corrections with user setup corrections.
Results: In 159 MVCT studies of 14 patients with typical upper abdominal and retroperitoneal radiation target volumes, user setup corrections were required for optimized target setup in 84.3%. Mean absolute x, y, z corrections suggested by MI fusion were 3.1, 4.4, and 7.8 mm; mean rotation was 0.5 degrees. Mean respective user setup corrections were 3.7, 5.9, and 9.2 mm, with rotations of 1.0 degree. The mean 3D vector of setup correction was 10.6, and 13.1 mm by MI, and user assessment, respectively. Differences in 3D vector length between automated and user setup exceeded 5, 10, and 15 mm in 25%, 11.2%, and 3.9%, respectively. Automated MI fusion provided on average 76% of the setup correction established by the expert user. MVCT image quality did not allow assessment of MI fusion quality in 7/159 attempts (4.4%). MVCT image quality was judged good, fair and poor in 71 (46.7%), 66 (43.4%), and 15 (9.9%) of the remaining attempts. Operative clips aided in establishing appropriate setup, while gas in stomach and bowel caused detriments in image quality. Targets embedded into soft tissue organs such as liver metastases and hepatobiliary tumors were generally poorly visualized.
Conclusion: Despite the limited soft-tissue contrast, MVCT can be a valid imaging modality for image-guidance of upper abdominal and retroperitoneal soft-tissue radiation target volumes. However, in individual patients and in the absence of fiducials within the target volume, MVCT may fail to provide imaging allowing discerning a soft-tissue target volume. While the system integrated automated image-fusion provides for a seamless clinical workflow, expert user online target location assessment was frequently needed to derive an optimal target setup for tomotherapy delivery.

911 POSTER

Changes in the process of care for small-cell lung cancer (SCLC): Results of the 99-01 Patterns of Care Study (PCS) nationwide survey in Japan

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Background: This study was undertaken to evaluate evidence-based changes in the care process for small-cell lung cancer (SCLC) in Japan through the Patterns of Care Study (PCS) nationwide survey.
Materials and Methods: From July 2002, the PCS conducted a second nationwide survey of care process for stage I-III SCLC patients treated with thoracic radiotherapy (TRT) between 1999–2001. PCS investigated; (1) patient background, (2) work-up studies, (3) process of TRT, and (4) process of chemotherapy. Practice patterns of 99−01 PCS were compared with those of 95−97 PCS.
Results: By using two-stage cluster sampling, the PCS collected data for 139 eligible SCLC patients (men to women ratio, 5:1; median age, 69; age >70, 43%; KPS > 70, 73%; stage III, 89%). Pre-treatment work-up study included chest CT in 96%, fiberoptic scope in 93%, brain CT or MRI in 86%, bone scintigraphy in 79%. The median total dose of TRT was 5000 cGy. Twice-daily radiotherapy (BID) was used in 43%. The median field size of TRT was 12 × 14 cm, including ipsilateral hilus in 96%, ipsilateral mediastinum in 96%, contralateral mediastinum in 84%, and contralateral hilus in 17%. Field reduction during TRT course in 61%. The most predominantly used photon energy was 10 MV (77%), whereas obsolete technique using Co-60 or X-ray energy <6 MV comprised 12%. 3D-conformal therapy was used in 12%. Dose prescription was at an isodose line in 15%. CT-simulation was performed in 40%. Only 12 patients (9%) received prophylactic cranial irradiation (PCI). Ninety-two percent received systemic chemotherapy, of those, platinum based chemotherapy constituted 98%, and 73% were treated by concurrent chemoradiation (CCRT). Treatment by IRB-approved protocol was only 6 cases (4%). Compared with the previous 95−97 PCS, significant increases in the use of CCRT (37% to 73%, P < 0.0001 by Chi-square test), BID-TRT (19% to 43%, P < 0.0001), and PCI (2% to 9%, P = 0.01) in the management of SCLC could be detected, although the absolute number of patients receiving PCI was still extremely low.
Conclusions: Evidence-based CCRT and BID-TRT had well penetrated into clinical practice, however, PCI has not yet widely accepted in Japan.

912 POSTER

Linac based helical intensity modulated total body irradiation

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Background: Total body irradiation (TBI) is frequently used in a conditioning regimen for patients undergoing bone marrow transplantation. While achieving a high level of success, TBI does carry with it significant risk for early and late toxicity, particularly for lung. The ability to selectively lower radiation dose to the lungs may reduce the incidence of symptomatic and life-threatening pneumonitis and allow TBI to be used in cases where compromised lung function would have previously precluded this. We present a new linac based treatment modality for TBI, which allows us to limit dose to organs at risk such as lungs and kidneys, without compromising dose to the rest of the body.
Materials and Methods: Our technique makes use of a helical beam delivery path defined by simultaneous gantry rotation and couch translation. MLC leaf positions and dose-rate are derived using a novel aperture based optimization method. Potential advantages of this technique are (1) critical structures may be spared without compromising target coverage, (2) a conventional isocentric 6MV linac and standard treatment couch is used, (3) on-board kV imaging may be used to monitor patient position on a daily basis, (4) helical beam delivery eliminates the need to turn the patient from prone to supine as is currently required in some standard TBI delivery methods.
Results: We will present treatment planning results obtained for our Varian Clinac iX linac. The first objective is to reproduce the dose distribution achievable in our current TBI technique (uniform dose ±10% to the entire body using a Cobalt-60 sweeping beam). Next we develop optimization strategies that allow conformal avoidance of critical normal structures (rather than defining a limited target such as total marrow or lymphatic system, which may risk higher relapse rates).