the increase in WT might cause a bigger loss in tumor control and/or higher morbidity, with again a rise of health care costs.

926

Intensity Modulated Radiation Therapy (IMRT) in lung cancer

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For patients with limited disease (LD) small cell lung cancer (SCLC), accelerated radiation therapy (40–54 Gy/3–3.5 weeks) applied simultaneously with the first or second cycle of full dose chemotherapy has lead to significant improvements in long-term survival in randomized trials[9, 5, 8]. However, a local relapse rate of 42–55% is an argument for radiation dose or dose-intensity escalation. In the randomized trials, an incidence of grade 3–4 acute esophageal toxicity of about 30% suggests that the maximum tolerated dose-intensity (MTDI) was reached for radiation. This was confirmed by Choi et al., who found that the MTDI was limited by acute esophageal toxicity at 45 Gy in 30 fractions over 19 days[2] in a phase I dose escalation trial of radiation simultaneously with chemotherapy in LD-SCLC. IMRT offers a window for dose(-intensity) escalation by its ability to generate intentionally inhomogeneous dose distributions from which i) the low-dose volume coincides with the location of the esophagus and ii) the dose intensity is consistent with the MTDI. The high-dose volume conforms to the tumour up to a dose-gradient zone at close distance from the esophagus. In locally advanced (LA) non-small cell lung cancer (NSCLC), dose escalation is limited at about 70 Gy by pulmonary toxicity when radiation only is used[7, 6, 11, 1]. Local control was less than 50% in these studies. With hyperfractionated accelerated radiotherapy or simultaneous radiochemotherapy, acute esophageal toxicity may become a second dose limiting factor[10, 12]. In planning studies, we have demonstrated that an assembly of parasagittal intensity modulated beams allowed 20–30% dose escalation (when compared to non-IMRT 3D-plans) at equitoxic levels for lung and spinal cord[3, 4]. With such promising news, why isn't IMRT investigated in dose escalation studies for LD-SCLC and LA-NSCLC? The answer lays in radiation-dose uncertainties in and around lung tissue, caused by inaccuracies of all conventional computation algorithms which are further aggravated by i) intensity variations in the beams and ii) narrow photon beam collimation. Inaccurate dose computation misguides the dose distribution optimization processes which are typical for IMRT. Monte carlo based dose computations are accurate and will allow safe introduction of IMRT for lung cancer as soon as more computer performance is widely available and the work-in-progress regarding the linear accelerator head modelling is finished

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927

Conformal radiotherapy of prostate cancer in clinical practice

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In three-dimensional conformal radiotherapy, the high-dose region is adapted in three dimensions to the shape of the tumor. The advantages are a reduction of acute and late side-effects. Furthermore, it is possible to raise the dose to the tumor, thereby potentially increasing tumor control rates. A prerequisite for conformal radiotherapy is a high geometrical accuracy. Geometrical uncertainties are mainly caused by deviations of the position of the tumor relative to the treatment portals. Three different sources of geometrical uncertainty can be distinguished: definition of the tumor volume, variations of the position of the tumor relative to the bony anatomy, and deviations of the set-up of the patient relative to the isocentre of the treatment.

Uncertainties in the definition of the prostate in MR and CT images were evaluated for 18 patients. The CT volumes were 40% larger than the MR volumes; the differences were mainly located at the apex and at the base of the seminal vesicles. This interscan variation was found to be larger than the interobserver variation.

The center of mass (CM) motion of prostate and seminal vesicles was studied, using repeat CT scans. The motion along the AP axis was larger than along the SI axis, while motion along the LR direction was small. The motion of the CM of the seminal vesicles was larger than the motion of the prostate. The systematic component (variation between patients) was larger than the random component (due to daily variations).

Patient setup deviations were studied using an electronic portal imaging device. Using the appropriate decision rules for setup corrections, the systematic component could be reduced substantially: the percentage of patients with a 3D systematic deviation larger than 5 mm was reduced from 30% to 1%.

The margin, necessary to account for these uncertainties amounts to 0.7 times the Standard Deviation (SD) of the total random component of the organ position variation. For the systematic component, the margin amounts to 2.0 - 2.5 times the SD of the total systematic component. Since tumor motion gives the largest contribution to the overall systematic deviation, reduction of margins can be obtained by reduction of the systematic component of tumor motion.

928

Current status of Hadrontherapy with carbon ion beams

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Purpose: Heavy ions possess advantageous dose localization at depth and RBE increases with increasing LET in depth, which gives the improved ratio of the 'biologically equivalent dose' between the peak and plateau. In addition, heavy ions are specifically efficient against hypoxic cells or cells in a resistant phase, and exhibit little repair of cells irradiated in the peak. The NIRS has been evaluating the efficacy of carbon ions generated by Heavy Ion Medical Accelerator in Chiba(HIMAC) in Phase I/II trials ongoing since 1994.

Methods: As of April 2001, more than 1000 patients are enrolled in the study. Of them, 829 patients who have a minimum follow-up of 6 months are analyzed. In Phase I/II dose-escalation trials, doses were escalated by 5~10% increments to provide for patient safety and determine appropriate RBE values.

Results: In this study the patients with locally advanced tumors and those with medically inoperable tumors were mainly treated. As with the radiation related morbidity, there were 5 patients (0.6%) who developed Grade 3 late skin reactions. Two patients developed acute pneumonitis with severe dyspnea at rest. For them steroid treatment was required with significant improvement. Of the patients whose GI tract was partially or totally irradiated in the initial trials, 16 patients developed serious complications of the esophagus or bowels. Among them 2 patients died of recurrence but the remaining 14 patients are alive and free of tumor. Two year local control rates were 60~80% for head and neck tumor, 62~86% for Stage I NSCLC, 80% for liver cancer, 97% for prostate carcinoma, 50~75% for uterine cervix carcinoma, and 75% for bone/soft tissue sarcomas.

Conclusions: Carbon ion therapy has shown promise against a variety of tumors that are hard to cure with other modalities. Tumors that responded favorably to carbon ions include non-squamous cell tumors such as adenoca, adenoid cystic ca, malignant melanoma, hepatoma, and bone/soft tissue sarcoma. Locally advanced tumors, slow-growing tumors, or medically inoperable tumors are also suited for carbon ion therapy. In treatment of parallel organ tumors the overall treatment schedule was successfully shortened to 1~3 weeks or even shorter, which minimized the proliferation of tumor cells during treatment.

929

Surgical treatment of metastatic disease: are the number of metastases a limit for surgical resection of lung metastases

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Surgery is a standard procedure for the treatment of lung metastases in selected patients with malignant tumors. The main selection criteria for candidates to such approach include the primary tumor type, duration of free interval between the initial tumor treatment and the lung relapse,