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and were administered at a rate of 2 ml/min. Groups of three animals each received one of three doses ranging from 150  $\mu$  Ci to 400  $\mu$  Ci intended to deliver 50, 100 or 150 Gy. An external magnetic field was focused on the tumor throughout the infusion and for 15 min following treatment to localize the microparticles to the area of interest. Radioactivity was measured in blood collected 30 min and 1 hr after dosing. Biodistribution of 90Y in the liver, lung, spleen, and bone was evaluated in three rabbits >24 hr after treatment. Remaining animals were recovered and kept for 7 days. Prior to necropsy and subsequent histopathological examination, animals were evaluated by CT to measure tumor size and MRI for particle localization. No embolization or adverse clinical signs were associated with magnetic targeted delivery of MTC-90 Y. Blood levels of radioactivity were  $\leq$  1% of  $^{90}\mathrm{Y}$  administered and decreased between 30 min and 1 hr. Organ levels of radioactivity measured >24 hr post-dosing showed the majority of the intra-arterially administered 90Y was localized in the liver with magnetic targeting. MRI performed 7 days after treatment showed the presence of the iron component of the MTC particles primarily in the liver tumors. Microscopic examination of tissue showed the presence of particles confined to the liver. Liver necrosis was greater in treated animals (> 70% necrosis) as compared to controls (50% necrosis). The highest dose resulted in complete destruction of the tumor as well as the underlying liver parenchyma, but it was limited to the left tumor-bearing lobe. This study suggests the feasibility of intra-tumoral radiotherapy using magnetic targeting and provides the foundation for additional investigations.

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#### Treatment margins and treatment fractionation in conformal radiotherapy of muscle-invading urinary bladder cancer

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**Background:** The size of daily doses and treatment margins varies greatly in conformal radiotherapy (CRT) of urinary bladder cancer. In this planning study dose-volume histogram (DVH) data and normal tissue complication probability (NTCP) predictions for intestine and rectum were compared for different combinations of clinically applied margin widths and fractionation schedules in bladder irradiation.

Material and Methods: Normal tissue dose distributions in fifteen bladder cancer patients treated with radical CRT were studied retrospectively, using standard three-field (Ant/Laterals) and four-field (Ant/Post/Laterals) beam configurations as model set-ups. The impact of margin width on the normal tissue dose distribution was initially evaluated using DVH data. NTCP modelling was used to compare the impact of choice of margin size and fractionation schedule. The analysis included CTV-PTV margin combinations of 1.0 cm isotropic (narrow margins) and 1.2-2.0 cm non-isotropic (wide margins) and fractionation schedule alternatives of 52.5 Gy/20, 55 Gy/20, 57.5 Gy/20 and 64 Gy/32.

**Results:** Using wide margins, the volumes of intestine and rectum receiving high doses increased by factors of approximately two and four, respectively, compared to using narrow margins. Similar factors between wide and narrow margins were also found for intestine and rectum NTCPs at the different fractionation alternatives, but the impact of margin size depended on the volume effect expressed by the NTCP model parameters. However, using standard NTCP parameters, the choice of margins and fractionation schedule had a similar impact on intestine NTCP predictions, while for the rectum, the choice of margin had a greater impact than the choice of fractionation. For a given choice of margin, the intestine and rectum NTCP predictions using 55 Gy/20 and 64 Gy/32 fractionation schedules were comparable. For clinics using narrow margins and a fractionation of 52.5 Gy/20, the NTCP modelling suggested that a moderate dose escalation (to 55 Gy/20 or 64 Gy/32) or changing to wide margins had a similar effect on the intestine and rectum NTCP predictions.

**Conclusion:** This modelling study of bladder irradiation suggested that the choice of margins was as important as the choice of fractionation in terms of intestine and rectum DVH parameters and NTCP predictions. The 55 Gy/20 and 64 Gy/32 fractionation schedules appeared to be comparable in terms of intestine and rectum NTCP predictions.

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#### Evaluation of cyberknife frameless real-time image-guided stereotactic radiosurgery for spinal lesions

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Background: The role of stereotactic radiosurgery for the treatment of intracranial lesions is well established. Its use for the treatment of spinal lesions has been limited by the availability of effective target immobilization devices. Conventional external beam radiotherapy lacks the precision to allow delivery of large doses of radiation near radiosensitive structures such as the spinal cord. This study evaluated a new image-guided frameless stereotactic radiosurgery delivery system known as the CyberKnife (Accuray, Inc., Sunnyvale, CA) for the treatment of spinal lesions with a single fraction radiosurgical technique.

Materials and Methods: This frameless image-guided radiosurgery system utilizes the coupling of an orthogonal pair of x-ray cameras to a dynamically manipulated robot-mounted 6-MV linear accelerator capable of six degrees of freedom that guides the therapy beam to the intended target without the use of frame-based fixation. Real-time image tracking allows for the tracking of patient movement with a 1-mm spatial accuracy. In this prospective cohort evaluation of a spine radiosurgery technique, 125 spinal lesions in 95 patients were treated with single fraction radiosurgery (45 cervical, 30 thoracic, 36 lumbar, and 14 sacral). There were 17 benign tumors and 108 metastatic lesions. Seventy-eight lesions had received prior external beam irradiation with maximum spinal cord doses. Cervical spine lesions were located and tracked relative to skull osseous landmarks; lower spinal lesions were tracked relative to percutaneously placed gold or stainless steal fiducial bone markers. All dose plans were calculated based upon CT images acquired using 1.25 mm slices. Planning treatment volume (PTV) was defined as the radiographic tumor volume with no margin.

Results: Tumor dose was maintained at 10-20 Gy to the 80% isodose line (mean 14 Gy). The maximum intratumoral dose ranged from 12.5 to 25 Gy (mean 17.5 Gy). Tumor volume ranged from 0.3 to 232 cc (mean 27.8 cc). The spinal canal volume receiving greater than 8 Gy ranged from 0.0 to 1.7 cc (mean 0.2 cc). Film dose measurement in a phantom demonstrated alignment of the treatment dose with the target volume to be within 1 mm. End-to-end tests revealed the planned dose never deviated more than 5% from the measured dose. Clinically, no acute radiation toxicity or new neurological deficits occurred during the follow-up period 3 24 mos (mean 12 mos).

Conclusions: Spinal stereotactic radiosurgery using a frameless image-guided system was found to be feasible, safe, and accurate. The major potential benefits of radiosurgical ablation of spinal lesions are short treatment time in an outpatient setting with rapid recovery and symptomatic response. This technique offers a successful alternative therapeutic modality for the treatment of a variety of spinal lesions not amenable to open surgical techniques, in medically inoperable patients, lesions located in previously irradiated sites, or as an adjunct to surgery.

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## High-dose rate versus low-dose rate intracavitary radiotherapy in the treatment of cervical carcinoma: a meta-analysis

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Background: Controversy still persists regarding the clinical efficacy of high dose rate (HDR) intracavitary radiotherapy (ICR), which was introduced in early 1960s, compared with conventional low dose rate (LDR) ICR in the treatment of cervical carcinoma. We performed meta-analysis to determine the effectiveness of HDR ICR compared to LDR ICR for overall survival, disease free survival, local recurrence, and complication rate of rectum and bladder in the treatment of cervical carcinoma.

Materials and Methods: We reviewed the literatures identified in searches of the Medline database, CancerLit database and the reference lists of the located articles from 1966 to Sep 2002 reporting treatment results of HDR and LDR ICR for cervical cancer. Fourteen published articles (3 prospective randomized trials and 11 retrospective studies) were selected by qualitative meta-analysis using inclusion and exclusion criteria for quantitative meta-analysis. The effective size (odds ratio) was obtained to compare 5-year overall survival, 5-year disease free survival, local recur-

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rence, and complication rate of rectum and bladder between HDR and LDR ICR in each study. Homogeneity tests were conducted before the integration of each effect size into a common effect size. The common effect sizes and 95% confidence intervals (CI) were calculated using either the fixed or the random effect model according to the results of the homogeneity tests.

Results: We performed meta-analysis with the data of 18,629 patients including 10,689 patients receiving HDR ICR and 7,940 patients receiving LDR ICR in 14 selected articles. The common effect sizes for 5-year survival rate, 5-year disease free survival rate and local recurrence rate were 1.1869 (95% CI: 0.9875-1.4264), 1.2037 (95% CI: 0.6284-2.3059), and 0.8926 (95% CI: 0.7330-1.0869). The common effect sizes for moderate to severe complication rates of rectum and bladder were 0.8625 (95% CI: 0.5877-1.2657) and 1.0937 (95% CI: 0.778-1.5375). There were no significant differences in 5-year overall survival, 5-year disease free survival, local recurrence and complication rates of rectum and bladder between HDR ICR and LDR ICR.

**Conclusions:** This study suggests that conventional LDR ICR could be replaced by HDR ICR which is safer and more convenient for patients and medical personnel. To determine the proper fractionation scheme for HDR ICR, additional well-designed prospective studies should be followed.

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## CT-based three-dimensional intracavitary brachytherapy planning in cervix cancer: Is it always better than conventional planning?

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**Background:** Intracavitary brachytherapy in cervix cancer is usually based on conventional orthogonal radiography-based planning (CP) notwithstanding the advances of imaging and three-dimensional planning technique (3DP). The purpose of this study is to compare CP with CT-based 3DP and to find the problems adapting 3DP into routine practice.

Materials and Methods: Thirty cervical cancer patients receiving Ir-192 HDR brachytherapy after external 30-40Gy RT were investigated. All patients underwent CT scanning and 3DP with CT images. For the CP, CT images, not orthogonal radiography, were used by digitizing point A, rectum, bladder points on CT to keep the same patient 's position and applicator geometry of two planning methods. Fractional 100% dose was prescribed to point A in CP and PTV (GTV+safety margin) in 3DP. Rectal-bladder ICRU and maximum point doses, volumes receiving 100% dose, surplus volumes (100% volume minus PTV) and rectal, bladder DVH were analyzed. The planning system PLATO was used.

Results: The mean pre-RT tumor size by MRI was 4.1cm. The mean volumes of GTV, PTV, rectum and bladder were 15.6, 31.5, 72.3 and 127.4cm3, respectively. Patients were divided into Group A and B by which 100% isodose line prescribed to point A fully encompasses PTV or not. The number of Group A patients whose PTVs are fully surrounded by 100% line was 20 and Group B was 10. The mean GTV (11.6 cm3) and PTV (24.9 cm<sup>3</sup>) of Group A were smaller than those (23.7, 44.7 cm<sup>3</sup>) of Group B (p=0.003). For the CP, the results of point doses and volumes showed no difference between two groups. For the 3DP, Group B suffered from large normal tissue doses and volumes significantly (p<0.05). In comparison between CP and 3DP in all 30 patients, though the mean 100% dose volume and surplus volume of 3DP were smaller (p=0.003 and 0.004), the results of organs at risk showed no difference except dose % irradiating to 50% volume of bladder (CP 36.4% vs 3DP 27.2%, p=0.03). In Group A, 3DP showed significant superior results to CP including organs at risk doses and volumes (p<0.05). However, in Group B with large tumors, the mean rectal and bladder irradiating doses and volumes were much higher in 3DP (p<0.05).

Conclusions: Although CP with point A prescription generally overestimates PTV, CT-based 3DP gives too much irradiation to organs at risk in large turnors. Other technique including interstitial implant or dose supplement to PTV without organs at risk should be considered in these cases. 500 POSTER

Dosimetric study of boron neutron capture therapy (BNCT) for multiple liver tumors: dose-volume histogram analyses using the simulation environment for radiotherapy applications (SERA) treatment planning system

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Background: Using a rat liver tumor model, we have successfully selectively accumulated high 10-boron concentrations in experimental liver tumors by intra-arterial administration of borocaptate sodium (BSH)/lipiodol emulsion. The present study aimed to investigate the feasibility of treating multiple liver tumors with boron neutron capture therapy using BSH/lipiodol emulsion (BSH/lipiodol-BNCT), from the viewpoint of dosimetry using the Simulation Environment for Radiotherapy Applications (SERA) system; a currently available BNCT treatment planning system.

Material and methods: Computed tomography images of four patients with multiple liver tumors were incorporated into the SERA system. Three treatment plans for irradiating the whole liver with BSH/lipiodol-BNCT using two or three epithermal neutron beams in one fraction were generated for each patient. The beam directions were as follows; anterior-posterior (AP), anterior-right (AR), and anterior-right-posterior (ARP). The 10-boron concentrations in the tumor and the liver applied in the present study were 197.3 and 15.3 ppm, respectively; the levels were obtained from experimental studies in animals. For comparison among the treatment plans, all plans were normalized to deliver a mean dose of 5 gray-equivalent (Gy-Eq) to the whole liver. The mean doses and the therapeutic gain factors for the tumors, defined as minimum dose to the tumor / maximum dose to the liver, and the inhomogeneity index of the thermal neutron fluence for the whole liver, defined as maximum fluence - minimum fluence / mean fluence were evaluated in each plan.

**Results:** Dose volume histogram analyses were applied separately to tumors in the left and right lobes. The mean dose delivered to the tumors in the right lobe by ARP-beams was significantly higher than that by AP-beams (65.1  $\pm$  19.5 vs. 45.6  $\pm$  19.1 Gy-Eq). The therapeutic gain factor for the tumors in the right lobe by ARP-beams was significantly greater than those by AP- or AR-beams (6.1  $\pm$  2.1 vs. 3.8  $\pm$  1.8; and 6.1  $\pm$  2.1 vs. 4.5  $\pm$  2.1). The mean dose delivered to the tumors in the left lobe by AP-beam was 53.3  $\pm$  23.4 Gy-Eq, which was higher than 45.1  $\pm$  19.4 Gy-Eq by AR-beams or 39.9  $\pm$  15.5 Gy-Eq by ARP-beams, but not significantly. The therapeutic gain factors for the tumors in the left lobe were 3.8  $\pm$  2.4 (AP), 3.5  $\pm$  2.2 (AR) and 3.5  $\pm$  1.8 (ARP), respectively. The inhomogeneity index of the thermal neutron fluence for whole liver using ARP-beams was lower than those by AP- or AR-beams.

Conclusions: ARP-beams can deliver the most homogeneous distribution of thermal neutron fluence to the whole liver, and provide the greatest therapeutic gain factors for tumors in the right lobe, along with approximately equal therapeutic gain factors for tumors in the left lobe, compared with the AP- or AR- beams. From a dosimetric viewpoint, the BSH/lipiodol-BNCT treatment plan using three epithermal neutron beams is the most suitable for treatment of multiple liver tumors.

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# Effects of topographic distribution of small bowel and field sizes on acute diarrhea in gynecologic patients undergoing pelvis irradiation

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Background: To find the topographic distribution of the small bowel within target and correlate both target volume and small bowel amount of full dose and risk of diarrhea during pelvic irradiation in patients with gynecologic malignancies

Materials and Methods: We reviewed 295 patients with cervical or uterine cancer managed by 4-field pelvic irradiation from January 2000 through January 2003. According to contrast within small bowel in simulation films, we categorized small bowel volume of full dose as no volume within target (NVWT), small volume within target (SVWT), and large volume within target (LVWT) group. External pelvic irradiation (39.6-45 Gy/ 22-25 fractions) was delivered to all patients initially. For investigating effect of field size, we categorized fields as whole pelvic (WP), inadequate whole