Conclusions: Contralateral metastatic lymph nodes are located more caudal than ipsilateral metastatic lymph nodes, in case of oropharyngeal or hypopharyngeal carcinoma. The position of the most cranial ipsilateral metastatic lymph node can not be used as a prognostic factor for the location of the most cranial contralateral metastatic lymph node. In elective irradiation, lowering the border of the contralateral irradiation field with 20mm below the base of the skull might be considered. Lowering the border at the ipsilateral site is not advised.

492 POSTER

Quantitative description of late normal tissue complications after radiation therapy

H. Jung[1], V. Svoboda[1], W. Alberti[2], T. Herrmann[3]. [1] *Institute of Biophysics and Radiobiology, University Hospital Hamburg-Eppendorf, Hamburg, Germany;* [2] *Dept. of Radiotherapy and Radiooncology, University Hospital Hamburg-Eppendorf, Hamburg, Germany;* [3] *Dept. of Radiotherapy and Radiooncology, Technical University, Dresden, Germany*

Purpose: An increasing number of patients survive cancer after having received radiation therapy. Therefore, the occurrence of late normal tissue complications among long-term survivors is of particular concern.

Methods: Based on the analysis of our own data (Svoboda et al., Radiother. Oncol. 1999; 53: 177-187) and numerous data sets from published reports it was shown, that three types of kinetics might be identified for the incidence of late normal tissue complications occurring after radiation therapy, provided the percentage of patients being free from late effects is plotted as function of time after treatment (Jung et al., Radiother. Oncol. 2001; 61: 233-246): Type 1, purely exponential kinetics; type 2, exponential kinetics, the slope of which decreased exponentially with time; type 3, curves composed of two components, a fast initial decline followed by an exponential decrease.

Results: Analysis of further data showed, that the curves of type 2 may also be described by one exponential component and a constant fraction, in particular when the total doses applied were relatively inhomogeneous. The constant fraction may indicate, that a portion of the patients received relatively small doses for which the risk of developing late effects was virtually zero. Thus, type 2 kinetics may be regarded as a special case of type 1 kinetics. In one subgroup of the patients, late effects occurred at exponential kinetics, whereas in the second subgroup total radiation dose was so small that late side effects did not occur even for longer observation periods.

Conclusion: Our results indicate that the risk for the occurrence of late complications after irradiation may remain constant for many years, either for all patients treated or for a subgroup exposed to doses exceeding the tolerance limit of the tissue under consideration. – Supported by Roggenbuck Foundation, Hamburg.

493 POSTER

Three-dimensional conformal radiotherapy (3D-CRT) planning for prostate cancer: 3 vs 4 vs 6 fields plans

E. Gez, R. Bar-Deroma, V. Bakouche, Z. Bernstien, R. Carmi, A. Kuten. *Rambam Medical Center, Oncology, Haifa, Israel*

Introduction: Radiotherapy is an effective treatment for localized prostate cancer. 3D-CRT planning makes it possible to increase the tumor dose and decrease the local toxicity. The optimal 3D-CRT plan for prostate cancer has not yet been determined.

Aim of this study: To define the optimal 3D-CRT plan for localized prostate cancer, i.e., the plan that gives the lowest dose to the rectum, urinary bladder and hip joints

End Points: % of critical volume irradiated and the % of critical volume that received 75% of prescribed dose

Material and methods: 10 consecutive pts with T1-2,N0,M0 prostate cancer scheduled to receive radiotherapy underwent evaluation to define the optimal 3D-CRT. The first part of radiotherapy consisted of small pelvis volume, the prostate + seminal vesicles with 2 cm margins, usually 12 X 12cm, given by box technique for a total dose of 50Gy. The second part consisted of the prostate and base of seminal vesicles and was given by 3D CRT planning. Pts were CT-scanned in a supine position at 5-mm interval, 2 cm inferior to ischial tuberosities to the bottom of sacroiliac joint. Neither immobilization device nor contrast medium was used. No specific guides concerning the status of urinary bladder and rectum were given to the patients. Three different treatment plans were generated for each patient: 1) three-fields plan: one anterior and two posterior oblique (0^0, 115^0, 245^0) with wedge 30^0 in oblique fields; 2) four-fields plan: anterior, posterior and two lateral fields (0^0, 90^0, 180^0, 270^0) without wedges and 3) six-fields plan: 2 lateral, 2 anterior in oblique and 2 posterior in oblique fields (40^0, 90^0, 140^0, 220^0, 270^0, 320^0) with wedges 30^0 in oblique fields. DVH of the prostate and seminal vesicles and of the critical structures was generated and presented numerically and graphically.

Results: The mean critical volume irradiated by 3, 4 and 6 fields plans for the rectum was 66%, 63% and 63%, for urinary bladder 57%, 56% and 45% and for the femoral heads 20%, 31% and 27%, respectively. The % of critical volume that received 75% of the prescribed dose by 3, 4 and 6 fields plans for the rectum was 54%, 35% and 37% and for the urinary bladder 40%, 335 and 27%, respectively.

Conclusion: Six-fields 3D-CRT plan is recommended to reduce the irradiation dose to the urinary bladder and rectum. Three-fields 3D-CRT is recommended to reduce the irradiation dose to femoral heads.

494 POSTER

Combination of ibandronate and radiotherapy in metastatic bone disease – final results of a randomized phase II trial

O. Micke, D. Berning, U. Schäfer, F. Bruns, N. Willich. *Muenster University Hospital, Department of Radiotherapy, Muenster, Germany*

Background: This randomized phase II trial investigated the synergistic effects of local radiotherapy combined with intravenously infused ibandronate with different application schemes.

Material and methods: 52 patients with lytic bone metastases from various solid tumors were included in the study (28 female and 24 male patients with a median age of 56 years). Baseline ECOG-PS was 02. The minimum follow-up period was 10 months.

A total dose of 36 to 40 Gy was locally applied on painful metastases. Treatment group A received ibandronate 4mg i.v. on the first day of irradiation plus 3 mg i.v. every 28 days for one year. Group B received ibandronate 1 mg i.v. on day 1, 8, 15, and 22 of radiotherapy, and an additional 3 mg i.v. every 28 days for one year. The patients were randomly assigned to treatment groups A and B. Stratification was done according to histology.

Pain intensity was measured using a visual analogue scale (VAS). The need for analgesics was documented and recalcification was analyzed semi-quantitatively.

Results: The median baseline VAS score for all patients in the study was 8 (range 104) [group A: 8 (range 9-4); group B: 7 (range 10-4)]. Eight weeks after treatment initiation, the median VAS score was 1 (range 5-0) [group A: 0 (range 5-0); group B: 1 (range 5-0)]. At the time of final data analysis (minimum follow-up period 10 months), the median VAS score was 0 (range 5-0) [group A: 0 (range 5-0); group B: 0 (range 3-0)].

The median WHO analgesic score before treatment was 3 (range 51) [group A: 3 (range 4-1); group B: 3 (range 5-1)]. After 8 weeks of treatment, the median analgesic score was 1 (range 4-0) [group A: 1 (range 4-1); group B: 1 (range 3-0)]. At the time of final data analysis, the median analgesic score was 1 (range 3-0) [group A: 1 (range 3-0); group B: 0 (range 3-0)].

In group A, 7/26 patients demonstrated complete recalcification, 13/26 patients had a partial recalcification, and recalcification had begun in 6/26 patients. In group B, the numbers for complete, partial and initiation of recalcification were 9, 11 and 6 (out of 26) patients, respectively. The total recalcification rate was 40/52 (77%). Median survival in both groups was 11 months. There were no statistically significant differences between treatment groups in pain scores, analgesic scores, or recalcification rates. No side effects due to infusion of ibandronate were observed.

Conclusions: The combination of local radiotherapy and intravenously applied ibandronate leads to a fast and substantial pain relief, which is maintained in the long-term.

495 POSTER

Targeted delivery of radioactive magnetic carriers in a rabbit liver tumor model

J. Geschwind[1], H. Kobeiter[1], M. Abusedera[1], C. Peterson[2], G. Tapolsky[2], T. Leakakos[2]. [1] *Johns Hopkins Hospital, Cardiovascular and Interventional Radiology, Baltimore, MD, USA;* [2] *FeRx Inc., Preclinical Development, San Diego, CA, USA*

Magnetic targeted delivery of the radionuclide, ^{90}Y, was investigated in liver-implanted rabbit tumors as a means of localized radiotherapy. CT scans and fluoroscopy were used to confirm VX2 tumor development. Rabbits were anesthetized and the left hepatic artery was selectively catheterized to within 2 cm of the tumor for a single intra-arterial infusion of either ^{90}Y labeled Magnetic Targeted Carriers (MTC-^{90}Y) or MTCs alone. The 5 ml infusions consisted of the radionuclide irreversibly bound to 25 mg MTCs

and were administered at a rate of 2 ml/min. Groups of three animals each received one of three doses ranging from 150 μ Ci to 400 μ 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 ^{90}Y 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 ≤ 1% of ^{90}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 ^{90}Y 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.

496 POSTER

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

L.P. Muren[1,2], A.T. Redpath[2], D.B. McLaren[3]. [1] *Haukeland University Hospital, Department of Oncology and Medical Physics, Bergen, Norway;* [2] *Western General Hospital, Directorate of Clinical Oncology, Department of Oncology Physics, Edinburgh, United Kingdom;* [3] *Western General Hospital, Directorate of Clinical Oncology, Department of Radiation Oncology, Edinburgh, United Kingdom*

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.

497 POSTER

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

P.C. Gerszten[1], C. Ozhasoglu[2], S.A. Burton[2], W.J. Vogel[2], B.A. Atkins[2], W.C. Welch[1], S. Kalnicki[2]. [1] *University of Pittsburgh Medical Center, Neurological Surgery, Pittsburgh, USA;* [2] *University of Pittsburgh Medical Center, Radiation Oncology, Pittsburgh, USA*

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.

498 POSTER

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

K.K. Lee[1], K.-R. Park[1], C.-B. Kim[2], C.-M. Nam[3], I.-J. Lee[1], J.-Y. Lee[1]. [1] *Yonsei University Wonju College of Medicine, Department of Radiation Oncology, Wonju, Korea;* [2] *Yonsei University Wonju College of Medicine, Department of Preventive Medicine, Wonju, Korea;* [3] *Yonsei University College of Medicine, Department of Preventive Medicine, Seoul, Korea*

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-