Conclusion: This preliminary study illustrates that selective PORT with tailored target volumes can be offered to patients after adequate curative surgery. It resulted in low geographical miss and was associated with a substantial reduction of the controlateral parotid dose.

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Human Papillomavirus (HPV) status in advanced cervical cancer: predictive and prognostic significance for curative radiation treatment

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Purpose: HPV infection plays a major role in oncogenesis of squamous cell carcinoma of the cervix. This study was performed to investigate if HPV status and E2 gene integrity are prognostic parameters for clinical outcome and predictive for radiation response.

Materials and Methods: Paraffin embedded biopsies of 40 women with locally advanced cervical cancer treated with curative radiotherapy were analysed for HPV infection and E2 gene integrity by multiplex PCR. Statistical analyses were performed for overall survival (OS), disease free survival (DFS), local progression free survival (LPFS) and treatment response (clinical complete remission CCR). Tested parameters were: HPV, median hemoglobin level, nodal status, median age, FIGO stage, grade, median RT dose. Same endpoints were used in regard to analysis of the E2 gene integrity.

Results: Twenty-eight (70%) of 40 carcinomas were HPV positive. The only significant factor for a better OS, DFS and LPFS was HPV positivity ($p < 0.02$, $p = 0.02$, and $p < 0.05$, log rank, respectively). HPV positive tumors had a significant better clinical complete remission compared to the negative group (67% vs. 33%, $p = 0.04$, Fisher's exact test). Patients with an intact E2 gene region showed a trend for a better DFS ($p = 0.1$, log rank)

Conclusion: This study reveals HPV as an independent prognostic parameter for clinical outcome and as a predictive factor for radiation response. The integration of the virus genome into the host cell DNA might be a molecular target to determine treatment response of HPV positive cancers.

490 POSTER

Exploiting the advantages of real-time intraoperative ctv definition: first report of an institutional phase I-II trial of perioperative fractionated HDR brachytherapy (PHDRB)

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Background: To determine the feasibility of a 4Gy bid PHDRB regimen. Protocol characteristics included: 1) implantation of catheters during open surgery; 2) CT-based dosimetry following the rules of the Paris system with manual optimization, 3) PHDRB dose assignment according to the quality of the surgical resection (R0 vs. R1 vs. R2) as described in the final pathology report.

Material and Methods: 111 patients have been included during the study period 2000-2003. Main groups were head and neck 41, sarcomas 34, gynecologic 15, colorectal 9 and other 12. Resection type was categorized as R0, R1 and R2 in 21, 88 and 2 patients, respectively. R1 resections were close in 45 patients (average margin distance of 3.2mm) and microscopically positive in 43 patients.

29 previously irradiated patients were treated with surgical resection + PHDRB. No further external beam radiation (EBRT) was given. The brachytherapy dose was 4 Gy bid x 8 (32 Gy total dose) for R0 resections, 4 Gy bid x 10 (40 Gy total dose) for R1 resections and 4 Gy bid x 12 (48 Gy total dose) for R2 resections. 82 unirradiated patients (54 with primary disease, 28 with recurrent disease after surgery) patients were treated with surgical resection + PHDRB + EBRT. Brachytherapy dose was 4 Gy bid x 4 (16 Gy total dose) for R0 resections, 4 Gy bid x 6 (24 Gy total dose) for R1 resections and 4 Gy bid x 8 (32 Gy total dose) for R2 resections. Radiation treatment was completed with EBRT to 45 Gy in 25 treatments, 1.8Gy/day, 4 to 5 weeks after surgery (concomitant chemotherapy was added according to the specific disease site protocol).

Results: 108 out of 111 patients (97.3%) could be treated with the PHDRB implant as prescribed. In the remaining three patients, the catheters had to be removed before the end of the PHDRB course due to infection in two and displacement in one.

RTOG grade 1-2 and 3-5 complications that may be attributable to the use of PHDRB were seen in 2 and 14 patients, respectively. Out of the grade 3-5 complications, three were implant-related (bleeding upon removal in 1, need for catheter relocation in 2) and 11 radiation-related (neuropathy in 2, soft tissue necrosis in 4, pelvic bleeding in 4, ENT bleeding in 1). Five of the six patients who may have died as a consequence of PHDRB, 5 had recurrent disease, four after prior radiation.

Three-year local control was 89%, 98% in unirradiated patients and 58% in previously irradiated patients ($p=0.0001$). Regional control was 76%, 84% in unirradiated patients and 53% in previously irradiated patients ($p=0.0043$). Freedom from distant failure was 66%, 72% in unirradiated patients and 46% in previously irradiated patients ($p=0.0039$). Three-year local control was 100% for R0 resections and 87% for R1 resections ($p=0.16$).

Conclusions PHDRB can be safely used after surgical resection. Three-year local control rates are excellent even after R1 resections, both in unirradiated and previously irradiated patients.

491 POSTER

Location of cervical lymph node metastases in oropharyngeal and hypopharyngeal carcinoma: implications for cranial irradiation field borders.

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Background: The objective of this study was to analyse the exact location of the most cranial metastatic cervical lymph node in patients with oropharyngeal or hypopharyngeal carcinoma. This was done in order to specify the cranial border of the irradiation field for improvement of parotid sparing irradiation.

Material and methods: The most cranial metastatic lymph node, ipsilateral and when present contralateral, was delineated on 58 diagnostic CT scans of patients with node positive oropharyngeal or hypopharyngeal carcinoma. The delineation was done in a truly three-dimensional fashion, using in-house developed software. The distances from the external border of the delineated lymph node to the base of the skull were measured in all planes.

Results: Forty patients with oropharyngeal and 18 patients with hypopharyngeal carcinoma were studied. In total 58 ipsilateral and 27 contralateral cervical lymph nodes were delineated. The mean distance to the base of the skull in the coronal plane was 25.6mm (range 2.6-73.8mm; SD 14.7) and 34.7mm (range 10.4-78.9mm; SD 14.0), ipsilateral and contralateral respectively ($p=0.002$). None of the patients with already advanced neck disease had the top of the highest contralateral metastatic lymph node within a distance of less than 10mm from the base of the skull, 5% less than 20mm, and 17% less than 30mm. This in contrast with the top of the ipsilateral metastatic lymph nodes, of which 15% had a distance of less than 10mm from the base of the skull, and 41% less than 20mm. No correlation was found between the location of the delineated lymph node and its volume, tumor type, T status, N status, or gender.

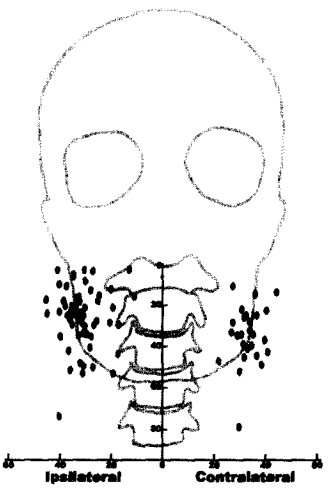

Figure 1. Schematic presentation of the most cranial metastatic lymph nodes. The crossing points of the cranial and the medial outer border of the metastatic lymph nodes are presented as a black dot. A division has been made between the ipsilateral and contralateral nodes. Distances are given in millimetres.

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

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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

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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

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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

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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