ago. As a control group, the same tests were applied to 40 unirradiated patients who referred to the ophthalmology department for any reason.

Results: The median values of VEP latency, VEP amplitude, contrast sensitivity and the rate of visual field defect were significantly worse in the irradiation group ($p=0.06$, $p<0.001$, $p<0.001$ and $p=0.005$ respectively). There was no dose-response relationship in all tests when 50 Gy was the cut-off value. However a positive correlation between time interval after radiotherapy and VEP latency ($r=0.406$, $p=0.003$) and a negative correlation between time interval and contrast sensitivity ($r= -0.499$, $p<0.001$) was noted; no correlation could be established regarding VEP amplitude and time interval.

Conclusion: Radiation-induced injury to the anterior visual pathways could result in an increase in VEP latency and a decrease in VEP amplitude and contrast sensitivity. This injury seems to be a continuous process developing in time.

486 POSTER

Evaluation of the new hypoxic cell radiosensitizer doranidazole in a murine tumour and mouse normal tissue

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Background: Hypoxia is a major factor for tumour resistance to radiotherapy and considerable effort is still being made to find approaches to overcome this problem. The aim of this pre-clinical study was to assess the potential of the new nitroaromatic compound doranidazole (POLA Chemical Industries) as a tumour radiosensitiser.

Material and methods: A C3H mammary carcinoma grown in the right rear foot of female CDF1 mice was used and treated when at 200 mm^3 in size. Doranidazole was dissolved in saline and intravenously injected into mice at a constant volume of 0.02 ml/g. Radiation (240 kV x-rays) was locally administered to the tumours or normal feet of restrained non-anaesthetised animals. Tumour response was assessed by calculating the percentage of animals at each radiation dose showing local tumour control at 90 days and skin damage estimated from the percentage of mice developing moist desquamation in the foot 11-23 days after irradiation. Following logit analysis of the dose response curves the TCD50 (tumour) or MDD50 (skin) doses (radiation doses producing a response in 50% of treated mice) were estimated and from these a sensitizer enhancement ratio (SER; ratio of the TCD50 or MDD50 for radiation alone and radiation with drug) calculated. Statistical analysis was performed using a Chi-squared test ($p<0.05$).

Results: The TCD50 value ($\pm$ 95% confidence interval) for radiation alone was 53 Gy (51-55). Injecting doranidazole (200 mg/kg) at 0, 30 or 60 minutes prior to irradiation significantly enhanced radiation response with the greatest effect seen at the 30-minute interval [TCD50 = 40 Gy (37-44); SER = 1.3]. No enhancement was seen if doranidazole was injected after radiation. Injecting different drug doses 30 minutes prior to irradiation showed a clear linear dose-response relationship, with the SERs going from 1.1 at 50 mg/kg to 1.8 at 500 mg/kg. In skin, using the 200 mg/kg dose and a 30-minute interval, the SER was only 1.1.

Conclusions: Doranidazole at non-toxic doses significantly enhanced radiation response of this tumour in a manner that is consistent with a hypoxic cell sensitizer and did so to a much greater degree than was seen in a normal tissue.

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487 POSTER

Geographical miss of the primary target and nodes in adjuvant breast radiotherapy as assessed by open MRI scanning

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Background: Good radiotherapy requires accurate targeting. Adjuvant breast cancer radiotherapy is planned without benefit of modern three-dimensional imaging in many centres. Even specialised CT scanners that can collect three-dimensional anatomical information in the necessary treatment position fail to demonstrate the primary site without the use of surgical clips. Clips pose problems, both in their placement, and in their final position. Despite this, radiotherapy reduces the chance of local recurrence from about a third of all cases to less than 10%. Improvements in the delivery of radiotherapy may help to reduce long term morbidity and mortality. MRI gives exquisite soft tissue definition in multiple planes, without the use of contrast. The primary site, nodes, surgical cavities and organs at risk are easily identified in three-dimensions.

Materials and Methods: Patients were scanned in the conventional treatment position in an open MRI scanner, using positioning lasers. A Siemens Open 0.2 Tesla scanner was used, with distortion corrected automatically using data derived from in-house phantom studies. In addition to axial scans, sagittal and coronal views can be constructed. A series of 528 patients with early operable breast cancer following conservative surgery were set up in the conventional treatment position, using standard positioning lasers, starting in January 1997. The field margins marked were the midline and the mid-axillary line. A Clinical Target Volume (CTV) of 1.5 cm surrounding the post-surgical tumour cavity was chosen, and the degree of geographical miss was calculated.

Results: It was found that 57% of all cases were receiving half or less of the prescribed dose to at least part of this CTV. Visible axillary nodes received less than half the dose in 47% case: this rises to a total of 80% patients if the post-surgical axillary cavity is also taken into account. Excluding peri-cardial fat, 73% patients had more than half the prescribed dose to the myocardium. Some lung received 50% or more of the dose in 95% cases. The radiotherapy plans were subsequently amended. All boosts were targeted using MRI.

Conclusion: The apparent effectiveness of poorly targeted radiotherapy raises interesting speculation. Improving treatment related morbidity and mortality might improve survival. Recurrence rates observed in 542 patients treated over the last seven years with MR modified two-dimensional radiotherapy will be presented.

488 POSTER

Selective conformal post-operative radiotherapy in patients with head and neck squamous cell carcinoma (HNSCC). Could the "bath of X-rays" be avoided?

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Background: Indications for post-operative radiotherapy in patients with HNSCC have been well established over the years. For both technical and conceptual reasons, target volumes typically included the entire neck and the site of tumor resection. This study presents data on post-operative irradiation (PORT) where the target volumes have been tailored based on the surgical procedure and the pathologic report.

Materials and Methods: Between January 2000 and June 2002, 47 patients (35 males and 12 females) with HNSCC (22 oral cavity, 10 larynx, 8 oropharynx, 7 hypopharynx) were treated with curative surgery on the primary tumor and on the neck using recommended procedures (Robbins, Arch Otolaryngol Head Neck Surg. 1991). There were 26 pT1-pT2 tumors and 21 pT3-pT4 tumors. Thirty-four patients were pN+ and 12 pN0. Indications for PORT followed published recommendations (Peters, Int J Radiat Oncol Biol Phys. 1993). Moderate and high risk patients received 60 Gy (range 59.2-60.8 Gy) and 64 Gy (range 63.2-65.7 Gy), respectively. Selection of targets volumes was tailored on the pathological finding, e.g. unilateral neck irradiation if pN0 on one side of the neck, or no neck irradiation in case of pN0 neck on both sides. Target volumes were delineated on a 3D basis using published guidelines (Grégoire, Radiother. Oncology, 2000). Planning was performed using forward planning IMRT. Typically, minimal dose to 95% of the PTV was 95% of the prescribed dose, and not more than 7% of the PTV received more than 107% of the prescribed dose. Maximum dose to the spinal cord was set at 50 Gy on the envelope. During the follow-up (FU) patients with loco-regional recurrence were imaged with CT, MR or FDG-PET and the relapse site was matched with the dose distribution of the planning CT scan.

Results: With a median FU of 16.6 months (5.1-34.9), 2 year actuarial loco-regional control and overall survival reached 80% and 68%, respectively. Presence of pathological lymph node infiltration, extracapsular spread and R1 resection were adverse prognostic factors, although they did not reach the level of significance due to the small number of patients. Two patients experienced a progressive disease in the target volume during PORT. Seven patients experienced a loco-regional relapse (1 local and 6 regional) within 1 year following surgery. In 3 of these patients, the relapse occurred outside the target volume (dose < 25 Gy). In 2 of these patients, relapses occurred at the same time outside the target volume (dose <25 Gy) and inside the target volume. In 46 patients, the mean dose to the controlateral parotid was below 30 Gy (range 1.7-33.8 Gy).

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.

489 POSTER

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.

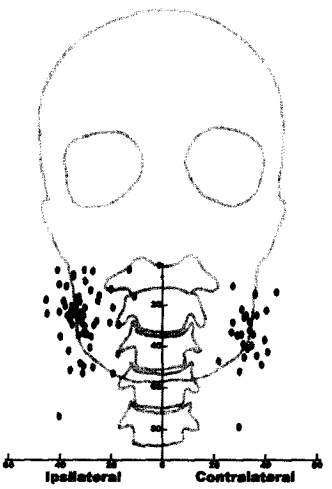

Figure 1. Schematic presentation of the most cranial metastatic lymph nodes. The crossing points of the cranial and the medial outer border of the metastatic lymph nodes are presented as a black dot. A division has been made between the ipsilateral and contralateral nodes. Distances are given in millimetres.