choice. A novel approach is the using of Extracorporeal Shock Wave Therapy (ESWT) if the established treatment schedules have failed. So far there has been no controlled study comparing the effectiveness of ESWT with an established conservative therapy such as X-ray stimulation irradiation.

Method: Thirty patients with chronic supraspinatus tendinitis were admitted into this prospective randomised study. After randomisation the patients were treated either with low dose radiotherapy or with ESWT. Irradiation was performed using a cobalt 60 unit. The applied was 6 times 0.5 Gy and was delivered to the ICRU reference point (1 fraction/day) with cobalt 60 gamma rays. ESWT treatment occurred three times with 2000 pulses per session (energy flux density ED+ 0.1mJ/mm2) in one week intervals using a Storz Minilith SL1. Primary endpoint was the age-corrected constant score.

Results: In the radiotherapy group average the age-corrected constant score improved from 38.6 before radiotherapy through 63.9 points after 12 weeks to 70.4 points after 52 weeks. In the ESWT group it rose from 41.5 points to 76.4 points and 81.9 points, respectively.

Conclusion: No statistically significant differences were proven between radiotherapy and ESWT. ESWT appears to be equivalent but not superior to radiotherapy in treating chronic supraspinatus tendinitis syndrome. A comprehensive randomised study is however necessary to ensure the equivalence of ESWT.

727 POSTER

Radiotherapy for age-related macula disease: a longitudinal single-arm study

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Purpose: To study the benefit from low dose fractionated radiotherapy in age-related macula disease (ARMD).

Methods: From 1997 to 1998, 72 patients with ARMD were enrolled. Patients with advanced cataract or concurrent retinal disease were excluded. 8 x 2Gy were administered to one eye in each patient. Fluorescein angiography and measurements of visual acuity were performed prior to, 3 mo., 6 mo., and 12 months after therapy. From 69 patients (30 classic ARMD, 39 occult ARMD) complete follow up data of at least 1 year were accessible to evaluation. The Wilcoxon rank test adjusted to serial tests (Bonferoni-Holm-method) was used to establish statistical significance. Acute and chronic potential side effects were also registered.

Results: The visual acuity decreased during follow up in 43/69, was stable in 18, and improved in 8 cases. The mean visual acuity deteriorated significantly (p=0.02). This holds true of both subtypes of ARMD. The most pronounced decrease of visual acuity occurred within the first 3 weeks. Occult ARMD did significantly better than classic ARMD (p=0.03). Neither age (p=0.17) nor sex (p=0.2) significantly influenced prognosis. 4 patients reported transitional complaints. Opacifaction of the ocular lens was not observed.

Conclusion: Low dose fractionated radiotherapy with 16 Gy is well tolerated. However, visual acuity is not preserved in the majority of ARMD patients. Despite promising initial reports our disappointing findings are in accordance with an increasing number of negative randomized and non-randomized published trials.

728 POSTER

Hyperbaric oxygen does not enhance tumour growth and metastatic potential of the rhabdomyosarcoma R1H

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Purpose/Objective: There is concern that hyperbaric oxygen therapy might have cancer-enhancing properties. This analysis was performed to investigate whether hyperbaric oxygen affects tumour growth and influences metastatic potential in an experimental tumour system.

Material and Methods: WAG/Rij rats bearing the R1H rhabdomyosarcoma on the right flank were locally irradiated with 250 kV X-rays. The radiation dose ranged between 50-90Gy given in 22-30 fractions in an overall treatment time of six weeks. For radiation enhancement, animals inhaled room air under ambient conditions (n=38), or normobaric carbogen (95% O2; 5% CO2) (n=41), or hyperbaric oxygen at a pressure of 240kPa (n=41). The number of carbogen or oxygen exposures ranged between 2-30 (median: 6), and the oxygen exposure times were at least 10 minutes at treatment pressure. Animals were followed up to 150 days after the start of treatment. The incidence of local recurrence or metastatic lung disease was scored. Pulmonary metastases were verified by post mortem lung dissection. The time interval between tumour transplantation and first signs of lung metastases was analysed using Kaplan-Meier-statistics.

Results: Fourteen animals in air, 13 in carbogen and 10 in hyperbaric oxygen developed lung metastases. The median time interval for the occurrence of pulmonary metastases was 127 days (95%-CI: 101-153 days), 132 days (95%-CI: 116-148 days) and 137 days (95%-CI: 120-154 days) for air, carbogen and hyperbaric oxygen, respectively. In the Kaplan-Meier-analysis there were no differences between the three groups (log-rank-test>0.5).

Conclusion: Our data give no evidence that tumour growth and metastatic potential of the R1H rhabdomyosarcoma is enhanced by hyperbaric oxygen breathing.

729 POSTER

The role of postoperative radiotherapy in the management of merkel cell carcinoma

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Purpose: Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine tumor of the skin with a high potential of locoregional relapse after surgery alone. The value of radiotherapy (RT) for curative treatment strategies was evaluated.

Methods: From 1/1990 to 5/2000, 31 patients with MCC (13 men, 18 women, age 34 - 92 years) were treated at the University of Cologne, Germany. Primary tumor sites were: head and neck region 13 pts., limbs 13 pts., trunk 5 pts.. The tumors were stage I (primary tumor alone) in 26/31 pts., stage II (locoregional metastases) in 4/31 and stage III (distant metastases) in 1/31. Treatment consisted of surgery alone in 14/31 pts., adjuvant postoperative RT in 16/31 pts. (one with incomplete surgery), and definitive RT in 1 patient with a stage III tumor. Postoperatively, the median target dose was 55,5 Gy to the tumor region. Additional RT to the regional lymph nodes was applied in 7 pts. with a median target dose of 54 Gy.

Results: With a follow-up of 4 to 112 months (median 22 months) the median overall survival (OS) after first diagnosis was 32 months (95%-CI: 0-75 months) with a 3-year OS rate of 47% (95%-CI: 25-69%). 6/31 pts. relapsed locally after a median of 4 months, 10/31 pts. developed regional lymph node metastases, and 7/31 pts. distant metastases. 9 pts. died as a direct result of MCC. Locoregional control and disease-free survival were significantly improved for pts. with postoperative RT (p=0.023). Uni- and multivariate analysis revealed that tumor locations in the head and neck and the lack of postoperative RT are unfavorable prognostic factors.

Conclusion: Postoperative RT to the primary tumor region and regional lymphatics reduces significantly the risk for locoregional recurrence, especially for head and neck MCC. Prospective clinical trials should be performed to confirm these observations.

730 POSTER

Osteoradionecrosis of pelvic bones - a single institution experience

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Purpose: to assess the incidence and risk factors of pelvic fractures as a result of radiation therapy in women with gynecological cancer.

Methods and materials: We retrospectively reviewed 4016 female patients treated at our institute between 1980 and 1998 with megavoltage radiation with or without brachytherapy for cancer in the pelvic area. Eligible were patients with vulvar, vaginal, cervical, endometrial and Fallopian tube cancer. Median follow-up was 88 months (range 0-240). Emphasis was put on treatment-related and patient-related risk factors.

Results: 15 patients developed symptomatic bone fracture caused by osteoradionecrosis, which makes an overall incidence of 0,37 per cent. The diagnosis was based on anamnesis, clinical course and X-ray or CT

images reviewed by one experienced radiologist. Median time of onset was 44 months (range 6 - 197). All patients had pain as the first symptom. The only independent predictive factor for developing osteoradionecrosis was pre-existent osteoporosis. Other risk factors, including higher age, postmenopausal status or steroide treatment, are all related to osteoporosis. We didn't find any significant treatment-related predictive factor for pelvic osteoradionecrosis.

Conclusion: Patients with osteoporosis are at highest risk for developing osteoradionecrotic fractures after pelvic radiotherapy. More studies are needed to find out other endogenous predictive factors (e.g.TGF-beta).

731 POSTER

Time-dose-response relationships in patients with head and neck squamous cell carcinomas treated by surgery and postoperative radiotherapy

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Purpose: To define the influence of the dose and time on the response to treatment in postoperatively irradiated head and neck cancer patients and to establish a good prediction of failure.

Methods and Materials: From January 1985 to December 1995, 214 patients with histologically proven head and neck squamous cell carcinomas were irradiated after radical surgery or single tumour resection according to surgical and histopathologic findings. The total doses given ranged between 50–75 Gy to the primary bed tumour and between 42–56 Gy to the neck with fraction sizes of 1.7–2 Gy/day. The median length of the time interval between surgery and radiotherapy, time of irradiation and total treatment time was 81 days, 59 days and 139 days, respectively. The end-point analysed was the local-regional tumour control rate at the primary tumour bed and neck for 5 years from the beginning of radiotherapy. Univariate and multivariate analyses were used to determine predictors of failure from among the following studied variables: i) clinical stage (T/N) of the patients; ii) tumour grade; iii) neck surgery; iv) tumour margins; v) histological tumour nodal extension; vi) chemotherapy; vii) normalised total dose; viii) time interval between surgery and radiotherapy; ix) time of irradiation; and x) total treatment time.

Results: The actuarial 5 years tumour control rate for the entire group was 72%, and 92% of the patients who achieved local control are currently alive without disease. Tumour control was inversely related to T stage (83% for T_2 vs. 57% for T_4) and the probability of local control within each stage was dependent on the N status ($\geq$71% for T_3-T_4/N_0 vs. 31–44% for T_3-T_4/N_1-N_3). Histological N status and tumour margins, but not tumour grade, impacted significantly on tumour control. When local control was analysed as a function of the dose to the primary, a nonsignificant negative dose-response relationship was found. The total treatment time was a significant prognostic factor and the time interval between surgery and irradiation proved to be an independent predictor of failure.

732 POSTER

Improving the quality of care in a rural radiation oncology center through use of telemedicine

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Purpose: In 1998, in a rural region of the United States, a telemedicine system was used to link a community radiation oncology center with an academic center of medical excellence in an effort to improve care.

Methods and Materials: A tele-medicine system was installed in both centers to allow remote consultation and review of treatment related radiographs. A 3-D compatible treatment planning system and practice management software allowed on-line review of treatment plans and data. A comprehensive quality assurance program was instituted. In December of 2000, utilization of the tele-radiography system and the trend of quality assurance indicators were assessed.

Results: The teleradiography system was used for peer review of all cases. This system was also used for sub-specialty consultation in the treatment of uncommon malignancies. The integrated treatment planning system allowed the simulation and treatment planning for complicated cases to be performed in the academic center and then the treatment was delivered in the community center. Quality assurance parameters showed a positive trend. Treatment accuracy, as measured by the deviation between the central axis simulation and portal films, was assessed. In 1998, 96% of port films (2,828 of 2,949) were within 0.5 cm and 1% (23 of 2,949) were greater than 1.0 cm. In 2000, 97% (4,111 of 4,245) were within 0.5 cm and 0% (17 of 4,245) were greater than 1.0 cm. Discrepancies between prescribed and treated field parameters improved significantly, from 0.9% (84 events/9,632 patient visits) to 0.3% (25 events/10,162 patient visits) between 1998 and 2000. Physicist chart reviews revealed deviations of 5-10% from prescribed parameters in 1.1% (15 of 1,375) and >10% in 1.2% (16 of 1,375) of charts reviewed in 1998 and deviations of 5-10% in 0.0% (0 of 2,096) and >10% 0.7% (15 of 2,096) in 2000.

Conclusions: Objectively, quality assurance indicators revealed a modest, but measurable, improvement following incorporation of the rural center into a regional oncology network. Subjectively, the teleconferencing system was useful in obtaining expert advice in treating less common malignancies as well providing on-going opportunities for continuing education.

733 POSTER

The concentration-dependency of the radiosensitising effect of gemcitabine and the influence of the rescue agent amifostine in vitro

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Gemcitabine (dFdC) is an active antitumour agent with radiosensitising properties. Since the combined use of dFdC and radiotherapy (RT) also results in an increased toxicity, there is a need for optimisation of this combined approach. Cytoprotective agents might be utilised to reduce these toxic effects. In that respect, amifostine (ami) is one of the most promising cytoprotectors that in vivo selectively protects normal tissues against radiation- or chemotherapy-induced toxicities. We studied the concentration-dependency of the radiosensitising effect of dFdC and the combination of dFdC/RT with ami in various cell lines.

H292 and A549, two lung cancer cell lines, ECV304, a bladder cancer cell line and CAL-27, a carcinoma cell line of the tongue were used in this study. The cells were treated with 0, 1, 2, 4, 6 and 8 nM dFdC for 24 hrs prior to RT. Ami (3.5 mM) and alkaline phosphatase (7.5 U/ml) were added 30 min prior to RT. Cells were irradiated at room temperature by 60Co over a dose range of 0-8 Gy. Cell survival was determined 7 days after RT by the sulforhodamine B test. ID50, radiation dose resulting in 50% cell kill was calculated from the survival curves, fitted according to the linear-quadratic model: survival=exp(-aD-bD2). The radiosensitising effect is reflected by the dose enhancement factor (DEF): ID50(-dFdC)/ID50(+dFdC). The protection factor (PF) was calculated by ID50(+ami)/ID50(-ami).

For ECV304 cells the DEFs varied from 1.39 to 2.98 after treatment with 1 to 6 nM dFdC. H292, A549 and CAL-27 seemed to be less sensitive for the radiosensitising effect of dFdC, with DEFs ranging from 1.05 to 2.67, 1.02 to 2.52 and 1.06 to 2.52 for 1 to 8 nM dFdC, resp. H292, A549 and CAL-27 cells were also less sensitive for the cytotoxic effect of dFdC: IC50 values (conc. causing 50% cell kill) were 8.0, 9.0 and 8.9 nM in H292, A549 and CAL-27 cells, respectively, while in ECV304 the IC50 was 3.1 nM. In combination with dFdC/RT ami clearly showed a protective effect. In H292 cells the PF of ami after treatment with 4 nM dFdC/RT was 1.64 and with 8 nM dFdC the PF was 1.86.

In conclusion, we observed a concentration- and cell line-dependent radiosensitising effect of dFdC in vitro, which seemed to correlate with the sensitivity of the cell line for the cytotoxic effect of dFdC. Ami clearly showed protective effects. Since these protective effects seem to occur selectively in normal tissues ami should be used to further optimise dFdC/RT combinations.

734 POSTER

Loss of alkaline phosphatase expression in breast carcinoma: Implications in the amifostine selective cytoprotection

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Introduction: Amifostine (WR-2721) is an importance cytoprotective agent widely used in clinical oncology to protect normal tissues against radiation and chemotherapy. This is an inactive compound that becomes dephosphorylated to an active thiol (WR-1065) by the enzyme alkaline phosphatase (AF), abundantly found in the normal endothelium. Although a direct evidence is missing, it is believed that amifostine selectively protects normal tissues and not the tumors, as AF is down-regulated in the tumoral vasculature.