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PUBLICATION

OXYGENATION STATUS IN PRIMARY SQUAMOUS CELL CARCINOMAS OF HEAD AND NECK

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45 patients with primary head and neck tumors were investigated pretherapeutically. In 30 patients the tumors were located at the floor of the mouth, the tongue or the tonsil. In these cases pO₂ measurements were performed in general anesthesia during endoscopic procedure. In 15 patients large neck nodes (N2/N3) were investigated pretherapeutically and during split course radiochemotherapy. In general, the median pO₂ distribution ranged between 2.4 and 46.6 mmHg and showed marked tumor to tumor heterogeneity. The follow up investigations during split course radiochemotherapy (n = 15) showed a significant increase of the median pO₂ after the pause. The observed changes of tumor oxygenation during therapy will be discussed in detail with regard to their clinical relevance.

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PUBLICATION

HYPERTHERMIA-ENHANCED EFFECTIVENESS OF CISPLATIN IN UNTREATED VERSUS IRRADIATED RAT SOLID TUMOURS

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Hyperthermia (HT) enhances cytotoxicity of cisplatin (CDDP). If this enhancement is different in untreated versus irradiated tumours is not known. Therefore this animal study investigates the efficacy of combined CDDP and HT in untreated tumours compared to tumours regrowing after irradiation.

Pieces of R-1 rhabdomyosarcoma were subcutaneously implanted in the hind legs of Wag/Ry rats. After irradiation, the tumours regrew

to their original volumes within 16 days. Chemo-hyperthermic treatment of untreated tumours or irradiated tumours at day 16 after irradiation consisted of CDDP (6 mg/kg ip), HT (1 h at 43°C) or CDDP + HT (45 min interval). The experimental endpoint was tumour growth delay (TGD). In untreated tumours CDDP + HT resulted in a significantly larger TGD than CDDP alone (11.6 and 7.4 days respectively, $P = 0.0002$), while HT alone showed a 1-day TGD. Preliminary results in irradiated tumours indicate that CDDP + HT rendered a similar TGD as in untreated tumours, although the TGD after CDDP + HT was not significantly different from CDDP alone.

Our findings show that HT enhances the effectiveness of CDDP in R-1 tumours. Untreated tumours probably respond similar to CDDP + HT as compared to irradiated tumours.

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PUBLICATION

CONTINUOUS VS. SPLIT-COURSE IRRADIATION FOR LUNG CANCER. IMMUNOLOGICAL IMPLICATIONS

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The therapeutic irradiation for lung cancer causes profound disturbances of host's general immunocompetence, the cellular immunodepression being the dominant finding. It is thought that the split-course technique holds certain advantage over the continuous irradiation, since the former includes a period of 4 weeks between two courses, thus allowing the lymphopoietic system to recover to a certain degree. In this report, we compared the radiotherapy-due alterations of several cellular immunity parameters (the number and function of total T cells, active T cells and the cells of monocyte/macrophage lineage), immediately after the completion of either continuously (n = 13) or split course-irradiated (n = 12) lung cancer patients. All patients had received the total dose of 60 Gy. Both therapeutic techniques caused alterations of the parameters tested: the significant decrease of the total and active T cells and their lymphoproliferative response, while the phagocytosing activity and the number of mononuclear phagocytes were increased, the latter being affected to a lesser extent in split-course-treated patients. Our results suggest that both techniques have similar immunodepressant effect on the cellular immunity of lung cancer patients.

Soft tissue sarcomas

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ORAL

FIRST CLINICAL EXPERIENCE WITH A GROWING ENDOPROSTHESIS, A LIMB SAVING PROCEDURE IN CHILDREN (FILM—10 MIN)

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Purpose of the study: To perform the first clinical study with an extendable endoprosthesis that can be extended non-invasively for children with a malignant bone tumor in the leg.

Method: A 14-year old boy had an osteosarcoma at the distal metaphysis of the femur. The patient was first treated successfully by chemotherapy (cisplatin, doxorubicin, ifosfamide and high dose methotrexate). The operation followed a few weeks after chemotherapy courses. Enough muscle tissue could be preserved. Resection was followed by reconstruction with a new extendable modular endoprosthesis system. The growing endoprosthesis is powered magnetically. An electromagnet, rotating outside the leg, produces a magnetic field that causes rotation of a small permanent magnet in the prosthesis. The magnet drives a motion screw via a gearbox. When the motion screw rotates the inner and outer tube of the prosthesis are forced apart.

Results: Seven months after the operation there was a leg length discrepancy of 20 mm. The first extension was performed and resulted in 2 mm growth. Anaesthesia was not necessary. X-rays prior to and after the lengthening procedure were taken to demonstrate the increase in length of the endoprosthesis. Six weeks later the second extension of 5 mm was performed successfully. Further extensions of 5 mm will be

repeated every one or two months to adjust the discrepancy in length of both legs.

Conclusions: The first clinical experience with a growing endoprosthesis seems to be successful. The patient regained almost normal functioning of his leg. Future extensions will prevent a leg length difference.

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ORAL

10 YEARS EXPERIENCE OF ADJUVANT RADIATION THERAPY FOR LOCALISED ADULT SOFT TISSUE SARCOMAS

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Between January 1984 and December 1993, 119 adult patients (68 males and 51 females, median age 42.5 years) were treated at our institute for localised sarcoma of extravisceral soft tissue, by maximal conservative surgery followed by adjuvant radiation therapy. 30% had previously undergone surgery and relapsed. Sites affected were the extremities (63.5%), trunk wall (13%), retroperitoneum (9%) and head and neck (4%). Predominant histologies were MFH (27%) and Synovialosarcoma (19%). 85% of tumors were grade 2 or 3. Thirty-seven patients (31%) received chemotherapy. In 75% of the cases, radiation therapy was performed using standard techniques and doses of at least 45 Gy. Bifractionated radiotherapy (dose 45 Gy) was used for patients treated between 1989 and 1992 (25%).

Treatment evaluation was performed on 1st March, 1995. Median follow-up is 66 months. 24% of the patients relapsed locally, and 47%

developed metastatic disease. Median intervals between surgery and local or metastatic relapse were respectively 14 and 13 months. Overall actuarial survival and disease-free survival at 2 years are respectively 77 and 47%. Grade, tumor size, tumor depth, bony or neurovascular involvement as well as quality of surgery show significant effects on DFS. Considering prognosis, hyperfractionated radiotherapy did not seem to be superior to standard techniques.

Long term side-effects, although usually mild, occurred in 35% of the patients. Dose of therapy, but not size of treatment fields, positively influenced them.

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NEOADJUVANT SYSTEMIC CHEMOTHERAPY COMBINED WITH REGIONAL HYPERTHERMIA IN ADVANCED OR RECURRENT SOFT TISSUE SARCOMA: RESULTS OF THE RHT-91 STUDY

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From Nov. 1990 to Oct. 1994 a total of 97 (72% pretreated) adults with locally-advanced, nonmetastatic soft tissue sarcomas were entered in a protocol (RHT-91) involving regional hyperthermia (RHT) combined with systemic preoperative chemotherapy followed by surgery. Primary tumor grading (84 patients had grade II or III), tumor size (>8 cm) and/or extracompartmental tumor extension (46 patients), or local recurrences (51 patients) were defined as high-risk factors. RHT was produced by an electromagnetic regional heating device (BSD-2000 system). For systemic chemotherapy the 97 patients received etoposide/ifosfamide/doxorubicin (EIA) with RHT being given on day 1 and 4 in repeated cycles (EIA/RHT) every 3 weeks. By the cutoff date for this analysis (Oct. 1994), 70 patients had undergone surgery after receiving EIA chemotherapy combined with RHT; 60 tumors except 10 could be resected without amputation. In 27 patients no further surgical procedure was performed. In 92 evaluable patients, the clinical response rate is 34% (1 CR = complete, 15 PR = partial, 17 MR = minor). 41 patients showed stable disease (NC) and 18 patients showed tumor progression (PD). Pathologic response to preoperative thermochemotherapy was evaluable in 70 patients with 30 responders (=43%) having either >50% histologic necrosis (FHR) within the resected tumors (20 patients) or pathological complete response (pCR) at the time of surgery (10 patients). All patients received—whenever possible—adjuvant chemotherapy and postoperative radiation. At the cutoff date, best response was obtained by the strategy of the RHT-91 study in 40 patients (=41%) showing no evidence of disease (NED) (median observation time = 18 months). An updated report will be given in regard to overall survival for non chemo-pretreated ($n = 73$) and chemo-pretreated ($n = 24$) patients. The protocol of a randomized multicenter trial (RHT-95) in patients with primary or recurrent high-risk soft tissue sarcomas will be presented to further test the potential of preoperative thermochemotherapy compared to neoadjuvant chemotherapy alone in regard to local control and survival.

Supported by grant M19/88/Wi9 from the Deutsche Krebshilfe, Bonn.

847 ORAL
CONSERVATIVE LOCAL TREATMENT BY MULTIMODALITY THERAPY IN 361 ADULTS' SOFT TISSUE SARCOMA (STS)

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Methods: From 1975 to 1992, 361 patients (pts) had their initial treatment at Institut Bergonié for non metastatic STS. There were 210 males and 151 females at a mean age of 50 years (16–87 years). 59% of the tumours were localized in the extremities. All pathological slides have been centrally reviewed. Grading according to the FNCLCC system was: G1 (18%), G2 (44%), G3 (38%). The local treatment combined surgery and radiotherapy in 83% of the cases. Surgery was conservative when possible. Marginal surgery was performed in 45% of the cases, wide excision in 48%. Compartmental radiotherapy was performed at a dose of 50 Gy, associated with a local boost (external beam, intraoperative or brachytherapy) when surgery was marginal. Chemotherapy was given in 126 pts (35%), in 60 of whom preoperatively.

Results: Amputation was necessary in only 7 pts (2%). Complete remission was obtained in 97.5%. Severe local complications occurred in

26 patients (7.2%). With a median follow-up of 6 years (1–20 years) local recurrence occurred in 21.4% of the cases, and metastasis in 28.7%. Actuarial 5-year overall and disease free survival are 66% and 59%. The function of the treated members was good in 92% of the pts. In univariate analysis, no difference was seen in local recurrence after marginal vs large excision when radiotherapy was done.

Conclusion: These treatment results compare favourably to those found in the literature. Satisfying functional outcome without amputation can be obtained by a multidisciplinary treatment approach.

848 ORAL
DOCETAXEL (TAXOTERE) AS FIRST LINE THERAPY FOR METASTATIC OR RECURRENT SOFT TISSUE SARCOMA (STS): A PHASE II TRIAL

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The clinical trials group of the National Cancer Institute of Canada is performing a multi-institutional phase II study of docetaxel in patients (pt) with measurable metastatic or recurrent sts with no prior systemic therapy. The starting dose is 100 mg/m² q 3 weeks with dose reduction for severe toxicities. Premedication includes 20 mg oral (po) dexamethasone (D) at 12 and 6 hours (hr) before, 50 mg diphenhydramine and 50 mg ranitidine both iv 1/2 hr before a 1 hr infusion docetaxel followed by 8 mg D po every 12 hr for 6 doses.

To date 22 pt have been entered, 1 is ineligible, 6 are too early for evaluation, 13 are evaluable for response and 15 for toxicity. Two partial responses and 6 stable disease have been reported. There have been 2 deaths on study unrelated to drug toxicity. The most common side effects have been: grade III–IV neutropenia (25/32 courses) with a median nadir of $0.4 \times 10^9/l$ granulocytes; five cases of febrile neutropenia and two with severe infection. There have been five hypersensitivity reactions only one severe. Mild-moderate lethargy (10 pt) and edema (5 pt) have also been seen. The median delivered dose intensity is 33.14 mg/m².

Because two responses have been documented the trial will continue until 30 evaluable pt have been entered. At the current rate of accrual it is expected that the final response rates and toxicities will be available by the time of presentation.

849 ORAL
PRELIMINARY REPORT OF A RANDOMIZED PHASE II STUDY COMPARING TWO DIFFERENT IFOSFAMIDE (IF) REGIMENS IN ADVANCED SOFT TISSUE SARCOMA PATIENTS (PTS) FAILING FIRST-LINE ANTHRACYCLINES

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Soft tissue sarcomas (STS) constitute 1% of all malignant tumors. Despite optimal local treatment 50% of pts will relapse. First-line chemotherapy is Ddoxorubicin 75 mg/m². The STS group performed a large ph 3 study comparing different anthracyclines. Patients failing at that study were eligible and randomized to receive (a) If 5 g/m² over 24 hrs or (b) If 3 g/m² in 4 hrs d 1–3 q 3 wks, both with adequate Mesna protection. A total of 86 pts of whom 78 evaluable and 66 off study were entered. Age 50 yrs (22–75), M = F, PS: 27:0, 51:1. Leyomyosarcoma 30/78. **Results:** 34 PD, 1 CR on A, 1 CR and 2 PR on B, RR 3 resp. 8%. No change (NC) resp. 9 and 17 pts. So progression arrest (Resp + NC) 35% with (a) and 53% with (b). **Toxicity:** both gr 3 + 4 leucopenia and thrombocytopenia were more pronounced with B: 33 vs 68% and 3 vs 15% and nadirs of Wbc 3.1 vs 1.35, Pt 203 vs 169.10⁹/l. Non hem. tox. did not differ substantially.

Conclusion: Higher IF results in more progression arrest and more manageable toxicity, but the overall response rate is disappointing.

850 ORAL
POST-RADIATION SARCOMAS: PRESENTATION OF A SERIES OF 116 CASES

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Post-radiation sarcomas are a rare and late complication of radiation treatment. The majority of them develops after 10 years.