RTh 07**SYMPTOMATIC RADIO THERAPY OF BONE METASTASES**

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In a pilot study 91 pat. with bone infiltration or metastases of various primary tumours were treated. Irradiation was carried out using photons or fast electrons. Five dosage and fractionation schemes were used: 1. 40 Gy in 20 fract. ov. 4 weeks (49 cases); 2. 30 Gy in 15 fract. ov. 3 weeks (6 cases); 3. 20 Gy in 5 fract. ov. 1 week (20 cases); 4. 20 Gy in 5 fract. ov. 1 week + 10 Gy in 5 fract. ov. 1 week (10 cases); 5. 50-60 Gy in 25-30 fract. ov. 5-6 weeks (6 cases). Account was taken of the degree and length of pain reduction, the general condition, restoration of mobility or ability to walk and recalcification. 71 patients (78%) with an average survival time of 38 weeks showed a positive reaction to the irradiation. The patients treated according to scheme Nr. 1 experienced in 46/49 cases (94%) relief of their complaints, lasting on average 25 weeks. The 6 pat. treated only with 30 Gy (scheme Nr. 2) all experienced pain-relief for approx. 28 weeks. In 80% (16) of the cases treated according to scheme 3 a palliative effect was observed, but only of 8 weeks duration. The further application of 10 Gy in 5 fractions (scheme 4) did not increase the pall. effect: in 6 of 10 cases (60%) pain-relief for an average of 13 weeks was achieved. The response-rate (100%) of the 6 pat. treated with 50-60 Gy and the average duration of remission of pain (24 weeks) are comparable with those of group 1 and 2. Summarising, the best palliative effects were achieved using schemes 1 and 2.

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RTh 08**SECONDARY MALIGNANCIES AFTER RADIO THERAPY: A RETROSPECTIVE ANALYSIS OF 454 CASES**

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The knowledge of radiation induced malignancies is mostly based only on case reports. We analyzed the data of 98 case reports (1902-1984) including 454 secondary malignancies (52% sarcomas, 38% carcinomas, 8,5% leukemias, two cases of brain tumours) after radiotherapy. Sarcomas occurred after irradiation with a dose of 12-70 Gy appearing more frequently after radiotherapy of malignant diseases (64%) than after radiotherapy of benign diseases (41%).

Carcinomas were mostly seen after irradiation with doses up to 30 Gy occurring more frequently after irradiation of benign diseases (57%) than of malignant diseases (30,7%). More carcinomas were observed after conventional irradiation (40%) than after ^{60}Co irradiation (25%). The percentage of thyroid carcinomas was remarkably high (60% of carcinomas), if the thyroid irradiation took place during childhood.

The occurrence of leukemias did not show any dose-relation. They appeared mainly after irradiation of malignant diseases (15%) than in case of benign diseases (2,7%). If radiotherapy was combined or followed by chemotherapy the percentage increased up to 42%.

The mean interval until diagnosis of the secondary malignancy varied between 7,1 years (leukemias), 12,1 years (sarcomas) and 19 years (carcinomas). Either additional chemotherapy as surgery as well reduced generally the interval: from 15,7 to 7,4 years (chemotherapy); from 18,7 to 11,4 years (surgery).

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NCy 01**TREATMENT OF SOLOID TUMORS AND ACUTE LEUKEMIAS WITH THE POLYAMINE ANTIMETABOLITES DIFLUOROMETHYLORNITHINE AND METHYLGLYOXAL BIS (GUANYLHYDRAZONE)**

M. Garbrecht, S. Busch, T. Langenbuch and G. Ziemer

A clinical phase II study was initiated to evaluate the efficacy of combination treatment with the polyamine anti-metabolites α -difluoromethylornithine (DFMO) and methylglyoxal bis(guanylhydrazine) (MGBG). Synergism of DFMO and MGBG in inhibiting tumor cell growth has been proven in different animal tumor cell systems (Biochem. Biophys. Acta 674, 169-177 (1981); Cancer 53, 1294-1298 (1984)). According to these data we initiated a clinical phase II study to evaluate the efficacy of DFMO+MGBG in patients (pts) with malignant melanoma, hypernephroma, testicular tumors, large bowel cancer, esophagus carcinoma and acute leukemias. All pts had received intensive prior treatment and showed progressive disease. 16 pts are evaluable. 3 pts had to stop DFMO-MGBG therapy because of severe side effects (myelosuppression 2, severe mucositis 1). 6 pts responded with partial remission (1-12 months), 4 pts showed stable disease (1-7 months). 6 pts did not respond. Partial remission or long term stable disease was seen in all of 5 pts with disseminated hypernephroma. Partial remission was also seen in 1 pt with AMML, 1 pt with esophagus carcinoma, 1 pt with melanoma and in 2 pts with large bowel cancer. Monitoring of polyamine excretion in the urine of pts revealed no significant reduction of putrescine. This might be due to interconversion of spermine and spermidine to putrescine as well as liberation of putrescine from necrotizing tumor. The fact that 10 pts responded with partial remission or showed long term stable disease despite poor prognosis and heavy pretreatment recommends further clinical investigation of the DFMO-MGBG combination chemotherapy.

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NCy 02**DECREASED CARDIOTOXICITY OF ADRIAMYCIN BY VERAPAMIL**

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Cardiomyopathy remains a problem in chemotherapy with Adriamycin (ADM) and other Anthracyclins. One out of several hypothetical ways to prevent ADM-cardiomyopathy is the use of calcium entry blockers such as Verapamil. Preliminary data of a pilot study which suggested benefit from the use of Verapamil as a 'protective' agent are now updated on the basis of a greater number of patients and an extended program of invasive and non-invasive investigations. The parameters of serial echocardiographical measurements of left ventricular pump function (shortening fraction: FS, peak fiber shortening velocity: V cf max) in patients treated with ADM and Verapamil (V) 3x40mg daily were compared with those of pts treated without V. The V group includes 35, the control group 61 pts. In the V group FS and V cf did not decline in the mean: d FS was + 0,026 FS%/100mgADM/sqm, d Vcf +0,0246 circ/sec/100mgADM/sqm whereas in the control group in the mean d FS and d Vcf showed a clear deterioration by - 3,4FS% and -0,33 circ/sec per 100 mg ADM/sqm (p: 0,001). Additional radionuclide ventriculograms proved good correlation with the echocardiographic data. In 4 pts with cumulative doses of ADM beyond 550mg/sqm endomyocardial biopsies were performed. The biopsy scores (according to Billingham classification) were 0,0,1,1 with FS rates at the time of biopsy of 34,34,30,-30% respectively. One of these pts subsequently developed clinically apparent cardiomyopathy under therapy with Mitoxantron. Pharmacokinetic studies in some of the pts showed that V 3x40mg daily did not change ADM disposition. The bioavailability of orally administered V however differs remarkably between individual pts.

The conclusions from the present data of this study are:

- (1) V probably prevents or delays myocardial damage caused by ADM.
- (2) The protective effect is presumably caused by prevention of cardiomyocyte calcium overload - an event which on the other hand is not specific for ADM-cardiomyopathy.
- (3) It seems questionable if 3x40 mg V daily is sufficient in all pts to achieve 'protective' serum levels.
- (4) Further investigations should be focused on the histopathological evidence of the postulated myocardial protection and on pharmacokinetic studies of V, ADM and their possible interaction.