

unexplored but could not be solved on this series. Prospective verification by large aperture CT image acquisition in treatment position using a simulator CT extension may be required.

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## PUBLICATION

### The preventive effect of verapamil on radiation induced cataract: An experimental study

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**Purpose:** Cataract formation is an unavoidable complication when radiation therapy, even in small doses, includes the lens. In this experimental study on rats, the preventive effect of verapamil, a calcium channel blocker, was studied on radiation induced cataract.

**Methods:** Experiment was performed on 40 female, 180–250 g weighted Wistar albino rats. Animals were divided into 3 groups. A control group (n = 10) was observed for 7.5 weeks. Radiation (n = 10) and verapamil groups (n = 20) which received 5 Gy radiation to whole cranium, in single fraction, including both eyes within irradiation volume, in addition verapamil group received daily subcutaneous injection of 8 mg/kg verapamil from the first day of radiation. At the end of 7.5 weeks all animals were sacrificed by bleeding. Ca, Na, K, levels were studied both in blood and in lens homogenates. Mg level could not be studied in sera for technical reasons.

**Results:** Serum levels of Ca, Na measured within normal ranges in all groups, but serum K level was higher than normal levels in control and radiation groups. Lens K and Na concentrations were not significantly different in control and radiation groups, but both levels were significantly lower in verapamil group (p = 0.0001, p = 0.0009). Ca levels were higher in the radiation group and lower in verapamil group compared to control ones (p < 0.0001). Mg levels were not significantly different (p = 0.590).

**Conclusion:** Verapamil effectively decreased the concentration of Ca in lens which is accepted as the key element in radiation cataractogenesis. Thus, it is concluded that verapamil may prevent radiation induced cataract formation.

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## PUBLICATION

### Is dosimetry by planning CT the optimal method for external beam irradiation of the breast?

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**Purpose:** In modern radiotherapy, the use of a planning CT for 3D dosimetry is widely spread. The reproducibility of the position of a patient being irradiated (IR) on the breast is difficult because of shape and composition of the breast and because of the position of shoulder and arm. Differences in position between simulation, planning CT and IR may occur. We therefore examined the possibility of these differences, their influence on treatment planning and dose calculation.

**Methods:** Forty pts with IR on the breast by two opposite fields were evaluated. Contours of the breast were taken after simulation and field markers were noted. The diameter between the center of both fields was measured. The size of the breast was measured by ultrasonography, which was used to complete the contours for 3D dosimetry. Each pt had a planning CT scan too, which was used for 3D dosimetry. Information of both was compared.

**Results:** Differences in diameter when measured by ultrasonography & contour and compared with reality were 0–3.5 mm. They occurred in ±80% and were not related to the size of the breast. There was no significant influence of these differences on dose calculations of the IR. The measurements by CTscan varied >80% and were almost always exaggerated. The differences in diameter ranged from 0–16 mm and were higher for pts with a greater size of breast. There was an influence of 0–6.4% on dosimetry and dose calculation.

**Conclusion:** The position of especially pts with a large size of breast is difficult to reproduce for simulation, planning CT and irradiation. This may cause a difference in dose calculation and total dose of the IR. For these pts, the dose calculations obtained by use of several contours and measurements of the breast size by ultrasonography might be more appropriate for dosimetry of external beam irradiation of the breast.

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## PUBLICATION

### The relations of radiation induced ultrastructural cardiac damage with serum troponin T and creatin kinase MB levels

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**Purpose:** Troponin-T (TnT) and creatin kinase MB (CK-MB) are specific markers of myocardial cell injury. Radiation-induced changes in the ultrastructure of the rat heart was shown but, relations of serum TnT and CK-MB levels were not investigated yet. This study was performed to search relationship between these markers and cardiac radiation damage.

**Method & Material:** In this time sequence study, wistar rats were exposed 20 Gy (200 kV, 0.5 Cu filter) irradiation to a field including the heart. The hearts were excised at varying time intervals (8 h–180 days) and the ultrastructure of myocardium was studied. Besides, serum TnT&CK-MB levels of irradiated and control groups were detected synchronously for every time interval.

**Results:** Changes were observed in myocytes at all time intervals. Although membranes of cells were intact, mitochondrial damage, characterized by swelling and fenestration, myofibrillar disarray and lysis, separation and damage of intercalated discs were seen focally. These changes increased progressively and we did not find any recovery in myocytes during the study period. TnT&CK-MB serum levels did not increase. In contrast TnT levels decreased in irradiated groups relative to control group at 24 h–180 days. CK-MB level decreased on the 60th day.

**Conclusion:** Radiation-induced cardiac myocyte damage did not cause an increase in serum TnT&CK-MB levels. But, these serum marker levels might be decreased by radiation induced cellular effects. These changes may be the result of intracellular radiation-mediated gene expression or extralysosomal protease activation.

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## PUBLICATION

### The efficiency of total liver irradiation (TLI) in patients with Hodgkin's disease (HD)

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**Purpose:** Involvement of the liver into pathologic process in HD frequently determines prognosis.

**Methods:** 37 patients with HD (liver lesions were proved by histology) were studied to estimate the efficiency of TLI in complex therapy. In 15 patients liver lesions were revealed during primary diagnosis of HD, in 22 patients liver lesions appeared in relapse of further progression. In all patients TLI was one of the stages of complete therapy and was held on gamma-apparatus. (Single dose was 1.8–2.2 Gy, standard fractioning 5 in a week, cumulative local dose 36–44 Gy).

**Results:** All 15 patients (1 group) were subjected to standard polychemotherapy (PCT) (MOPP or COPP), liver lesions eradication (LLE) was reached only in 4 patients, after TLI – in 14 from 15 patients. 11 patients live more than 5 years in remission. In 22 patients (2 group) LLE as a result of complex therapy, including TLI, was reached in 17 cases, but remission only in 13 cases. Life duration and prognosis in these patients depended only on the efficiency of PCT, but not TLI.

**Conclusion:** TLI is most useful when liver lesions appeared in HD manifestation. In HD relapse TLI is expedient if liver is the only single extranodal site, or if PCT is effective in other zones.

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## PUBLICATION

### Individualized vaginal moulds using 192-Iridium and CT evaluation in gynecological (Gyn) tumors

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**Purpose:** Individualized vaginal moulds along with CT-scan information to perform dosimetric study for low dose 192-Iridium (Ir) is a treatment modality used in Gyn cancer patients (ptes). We present a preliminary results of 15 ptes treated with this modality.

**Methods:** Since March 1995, 8 cervical cancer (6 stage IIA, 1 stage IV, 1 vaginal relapse) and 7 endometrial carcinoma (71% vaginal involvement) have been treated by vaginal moulds. All but one pte had surgery

mainly Wertheim-Meigs or total hysterectomy and bilateral anexectomy. After surgery 8 ptes had positive pap smear and 5 macroscopic residual disease. Twelve ptes treated with adjuvant external beam radiotherapy (EBR), (40–56 Gy), received between 15 and 25 Gy of low dose 192-Ir. In 2 ptes without EBR and in 1 re-irradiated pte, 60 Gy and 50 Gy were administered respectively in all cases the dose was administered at 0.5 cm from the vaginal mucosa. To optimize the dosimetric study, real-size CT slices (RSCTS) through the vaginal mould were performed the day after application.

**Results:** With a mean follow-up of 18 months, a complete response was obtained in 93% of ptes (14/15), with an actuarial local relapse free survival and overall survival of 78% and 90% respectively. One pte had progression within EBR and 2 ptes local relapse at 7 months. In 9 ptes the fat plane between the vaginal vault and rectum or bladder did not exist or the rectum was collapsed in the RSCTS. Complications: one vaginal stenosis (grade I), one hemorrhagic cystitis (reirradiated pte), 3 synechiae (grade I) and 9 telangiectasias (grade I).

**Conclusions:** 1. Even unfavorable clinical staging, the individualized low-dose rate 192-Ir vaginal moulds permitted to obtain a high local control with a low morbidity. 2. Probably Magnetic Resonance Imaging might provide more definition of soft tissues.

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## PUBLICATION

### The value of a 3-D-planning system for evaluation of lung dose in total body irradiation

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**Purpose:** Interstitial pneumonitis (IP) plays a prominent role in mortality after total body irradiation (TBI). For estimating the probability of IP the information of dose distribution in lung is of great importance.

**Methods:** Computed tomography (CT) scans were made through the thorax of 5 patients. With the information of the CT-scans and using a 3-D-planning system (TMS, Helax) individual volume-dose-histogramm, minimal and medium dose of lung were calculated for each patient. A multiple beam technique and a hyperfractionated regime (6 fractions of 2 Gy) were used.

**Results:** Median dose of right lung was 8.89–9.91 Gy (74.1%–82.6%), of left lung 8.72–9.65 Gy (72.7%–80.4%). Minimal dose, it means the dose, with 100% of the lung volume is irradiated with and which is important for estimating pulmonary damage, was 7.73–8.46 Gy (64.4%–70.5%) for the right lung and 7.66–8.69 Gy (63.8%–72.4%) for the left lung.

**Conclusion:** By Using a 3-D-planning system volume dose of the lung can be calculated and the probability of lung damage by TBI estimated.

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## PUBLICATION

### Ewing's sarcoma in childhood – The role of radiotherapy

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**Purpose:** Ewing's Sarcoma (ES) is a small, round cell tumour of childhood originating in bone. It is less frequent than osteosarcoma, representing 3% of pediatric cancer. Primary site was the most important prognostic factor reported in the analysis of IESS-I, being the pelvis the least favourable. Others includes, by the time of diagnosis, the presence of distant metastasis, serum levels of LDH > 350 U/l and a soft tissue involvement > 8 cm. We evaluated the importance of radiotherapy (RT) as an adjuvant therapy in the treatment of ES.

**Material and Methods:** From January 1978 to January 1995, 24 children under 15 years old, with the diagnosis of ES, were treated in our Department. We analysed the distribution by age and sex, presenting symptom, the primary tumor site, the adverse prognostic factors in the first evaluation, treatments done and follow-up results.

**Results:** Fifty-four percent were male and 46% female. The median age was 11 years (range 2–15). The presenting symptom was local pain in all children, followed by swelling in 20 cases. The primary tumour sites were: pelvis in 7 cases, tibia in 6, shoulder girdle in 3, femur in 2, hand bones in 2, rib in 1, humerus in 1 and temporal bone in 1 case. Fourteen children (58%) presented with 3 or 4 adverse prognostic factors. All cases were treated with a combination of chemotherapy (CT) and RT, and 4 cases (17%) underwent surgical resection. With a median follow-up period of 51 months (range 5–212), 42% of the cases are free from disease, corresponding to the patients that presented only 1 or 2 adverse prognostic factors in the first

evaluation. The patients who died in consequence of the disease, seven presented local tumor.

**Conclusions:** The importance of RT in the local control of these tumors is well established, as we could observe in our patients. However, the adverse prognostic factors had a great influence in the outcome of the children in the present study.

## Soft tissue & bone sarcomas

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ORAL

### Association of tumour growth on nude mice and poor outcome in soft tissue sarcoma (STS) patients

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**Purpose:** Human tumour xenografts do not represent the whole biological variability of a tumour entity, since successful establishment of permanently growing tumour cell lines cannot be achieved from all cancer patients. Permanent growth in nude mice (PGNM) maybe associated with poor clinical outcome. We tested this hypothesis in a group of STS patients.

**Methods:** Small chunks from fresh tumour biopsies of 81 patients with STS were transplanted subcutaneously into NMRI-nu/nu nude mice. Tumour cell lines exhibiting growth in nude mice for more than 3 tumour passages were considered as permanently established. Clinical outcome of all patients was monitored with an median follow up of 38 months.

**Results:** 42/81 (52%) STS exhibited PGNM. High grade, high S-phase proportion and aneuploidy were significant predictors of PGNM. Overall survival (OS) at 3 years was 21% (±8%) for STS patients with PGNM and 50% (±9%) for patients without PGNM ( $p < 0.01$ ). Considering only patients without distant metastasis at the time of biopsy ( $n = 49$ ), 3-year-OS was 25% (±17%) and 71% (±15%) for STS with PGNM and without PGNM, respectively ( $p = 0.02$ ). In a multivariate analysis, aneuploidy, PGNM, and tumour location at the trunc were independent factors associated with reduced survival time.

**Conclusion:** STS that are permanently growing on nude mice originate from patients with poor clinical outcome.

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ORAL

### Clinical impact of fusion transcripts detected in soft tissue liposarcoma and synovial sarcoma

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**Purpose:** Soft tissue sarcomas frequently express fusion transcripts encoded by gene fragments fused through translocation. We selected fusion transcripts of liposarcoma (FUS-TLS/CHOP), resulting from t(12;16)(q13;p11), and synovial sarcoma (SYT/SSX1-2) resulting from t(X;18)(p11.2;q11.2) to develop a polymerase chain reaction (PCR) based system for detecting minimal residual disease (MRD).

**Methods:** A nested PCR was established for both fusion transcripts. After RNA extraction of snap frozen tissue, peripheral blood or bone marrow aspirates, reverse transcription was carried out. We amplified the resulting cDNA with the nested PCR and analysed the product on agarose gels. 30 tissue samples of skin, blood, bone marrow and different soft tissue tumors served as controls. 23 patients with liposarcoma and 13 patients with synovial sarcoma were analysed.

**Results:** Of 23 liposarcomas investigated 8 revealed a fusion transcript. 11 of 13 suspected synovial sarcomas analysed showed a fusion transcript of identical length. None of the control tissues revealed a fusion transcript. Analysis for MRD revealed fusion transcripts in 1 of 4 intraoperative blood aspirates and 1 of 1 bone marrow aspirates.

**Conclusions:** Fusion transcripts of liposarcoma and synovial sarcoma are of potential benefit for gaining a definitive diagnosis in soft tissue sarcoma. Furthermore they can be useful in determining MRD.